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BLOOD IODINE STUDIES IN RELATION TO THYROID DISEASE*

Basic Concept Of The Relation Of Iodine To The Thyroid Gland; An Iodine Tolerance Test

BY H. J. PERKIN, B.S.,† FRANK H. LAHEY, M.D.,† AND RICHARD B. CATTELL, M.D.†

PART I

INTRODUCTION

IF some of the fundamental facts regarding thyroid secretion are discussed before the preliminary report of our experiences with blood iodine determinations and the iodine tolerance tests are recorded by H. J. Perkin, it will make it more readily possible for readers who have not been particularly interested in thyroid conditions to comprehend the remarks about blood iodine.

We have known now for a great many years that the secretion and secreting activity of the thyroid gland are intimately linked with iodine, that during its stages of overactivity the thyroid gland is in a state of hyperplasia and that during that stage there is an abnormally low content of iodine within the thyroid gland itself. (Marine and Lenhart[1], Cattell[2].)

It is possible now to extract by hydrolysis and precipitation a crystalline substance known as thyroxine (Kendall[3]) which has all of the physiological properties of thyroid extract. This active principle of the thyroid contains sixty-five per cent iodine and it is now quite generally accepted that the effectiveness of thyroid material to be employed therapeutically is proportional to its iodine content. It is, therefore, evident that the iodine content of the thyroid is related to the activity of that gland and is a probable indication as to whether the thyroid is storing its active principle or is pouring it out into the blood stream to stimulate the rapid heart action and increased metabolism observed in hyperthyroidism.

To understand the reasons why blood iodine is usually elevated in patients with excessive thyroid secretion (hyperthyroidism) and to grasp the basis of the blood iodine tolerance test as developed by Mr. Perkin, it is necessary to review some of the changes which take place in the thyroid during its secreting activity in hyperthyroidism (hyperplasia), the histologic and chemical changes which take place in the gland as the result of the administration of iodine (Lugol's solution) at this time (involution) and the relation of the histology in the normal gland to the iodine content.

The glandular unit of thyroid activity is a ring of epithelial cells surrounding an acinous overfilled (involution), moderately filled (normal) or scantily filled (hyperplastic—hyperthyroidism) with what probably represents the vehicle (colloid) containing the active principle of the thyroid secretion.

When the thyroid gland is secreting normally, it appears as shown in Figure 1. The epithelium lining the acinus will be flat cuboidal in character. There will be a moderate amount of colloid material within the acinus and the iodine content of the gland in terms of milligrams of iodine per gram of dried gland will be found to be within normal limits. (Approximately 2.0 milligrams.)

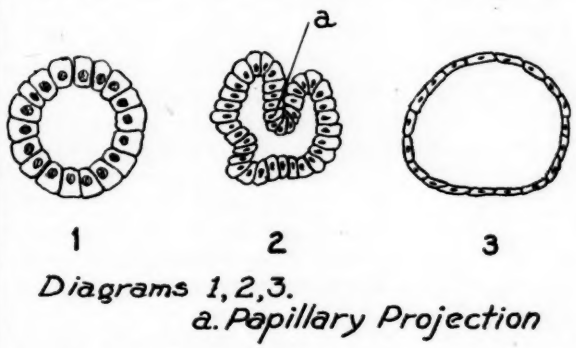

FIGURE 1. Diagrammatic representation of the normal thyroid unit. The acinus filled with a moderate amount of colloid and lined with normal cuboidal epithelium.

FIGURE 2. Diagrammatic representation of the thyroid unit in hyperthyroidism. Note the small amount of colloid within the acinus, the papillary projection (a) into the acinus and the columnar type of epithelium lining the acinus.

FIGURE 3. Diagrammatic representation of the thyroid unit of a patient with hyperthyroidism after treatment with iodine. Note the change designated as involution, a large amount of colloid in the acinus, dilatation of the acinus and flat inactive epithelium lining the acinus.

When a patient develops primary hyperthyroidism or exophthalmic goitre, then certain histologic and chemical changes take place within the thyroid gland and the epithelium surrounding the acinus becomes high columnar in char-

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acter, its acinar margin becomes crinkled and projects into the acinus in a papillary-like form and the amount of colloid in the acinus is impressively diminished, as shown in figure 2.

During this stage of hyperplasia and glandular activity, the iodine content of the thyroid drops strikingly in terms of milligrams of iodine per gram of dried gland until it is often as low as 0.4 of a milligram per gram of dried gland. (Marine and Lenhart[1], Cattell[2].) It is during the stage of excessive and abnormal thyroid activity that the thyroid gland discharges its contained iodine and it is in this state of thyroid abnormality that high values of iodine are found in the blood stream.

Since the iodine fraction of thyroxine is necessary to make it active, since the amount of colloid in the thyroid in the patient with hyperthyroidism is strikingly diminished, since the blood iodine in this state is found elevated and the iodine content of the thyroid low, one can, of course, theoretically assume that the increase in blood iodine is evidence of an increase in circulating thyroxine. That this is possibly so is made further probable by the information presented by Mr. Perkin in chart 3 in which the drop in blood iodine value, similar to the drops in metabolisms, are shown before operation, three months after operation and six months after operation.

If one now administers iodine (Lugol's solution) to the patient with excessive thyroid activity (hyperthyroidism) at this time very definite changes take place in the patient clinically, in the blood iodine, in the histologic appearances (involution) of the gland and in the iodine storage in the thyroid gland as shown in figure 3. The epithelial cells lining the acinus are flattened and within the acinus there accumulates a large amount of colloid material (involution). The blood iodine drops and the amount of iodine within the thyroid gland rises sharply until it may be as high as 8.0 milligrams of iodine per gram of dried gland. During this stage of involution there are, usually in 90 per cent of the cases (Cattell[2]), clinical evidences of relief as indicated by a drop in basal metabolism and pulse rate and a gain in weight. Having operated upon several thousands of thyroid glands during this stage of involution, we know also that there are gross changes in the gland at the time which, as the result of the accumulation of such large amounts of colloid in the acinus, are quite obvious to anyone experienced with thyroid surgery. The gland becomes strikingly firm, the vascular and lymph channels between the lobules, as the result of acinar distention, become for a time obstructed (Marine and Lenhart[1]), the vascularity of the gland diminishes and its diffusion of thyroxine through the lymphatics, because of their obstruction, also limited. This plus the possible mechanical effects of the pressure of excess colloid in the distended acinus upon the epithelial cells lining the acinus (Marine and Lenhart[1]) is the probable reason why involution as brought about by Lugol's solution or any other form of iodine results in such a prompt but temporary improvement in the clinical symptoms in patients with hyperthyroidism.

We have for years appreciated and maintained that the effects of iodine upon patients with hyperthyroidism were not to cure them of hyperthyroidism but to bring about a temporary improvement during which time surgery can be more safely carried out.

It is probable from the clinical course of patients with hyperthyroidism on iodine that the thyroid gland adapts itself to the distention of its acinus with colloid, that the temporarily restricted blood supply partly resumes its abnormal amount and that temporarily obstructed lymph channels as they adapt themselves to the new conditions are reopened (Marine and Lenhart[1]). This results then in a return of the severe symptoms of hyperthyroidism, increasing tachycardia, weight loss and increases in basal metabolism. Iodine becomes less effective in maintaining this clinical remission and the patient is then, so-called, iodine fast. The period of improvement during which the operation could have been more safely done has been lost, and it is not possible again to get the same striking iodine improvement in the patients even though they be taken off iodine for several weeks and put back on it again after this interval.

It is for the above reasons that we have always urged upon physicians that if their patients are not to be operated upon, they may give them all the iodine they choose, but if they are to be operated upon that they be sent to the surgeon not having had iodine, in order that he may give it to them, observe the period of maximum improvement and operate upon them thus with greater safety at that time.

To epitomize then our knowledge of iodine in hyperthyroidism exclusive of blood iodine: When we have hyperthyroidism with hyperplasia there is a low iodine content within the thyroid gland. At this time the gland leaks its iodine into the blood stream and is unable to store it. This hyperplastic gland of hyperthyroidism has, however, a tremendous thirst or affinity for iodine and if iodine, usually Lugol's solution, in any form be given at this time, it will promptly (literally within an hour or an hour and a half, see iodine tolerance charts) be accepted and stored in the gland as shown by the iodine tolerance curve. Following this within four to ten days, there will be a marked change in the thyroid gland (involution) which will result in a temporary improvement in the clinical picture of hyperthyroidism.

Part II

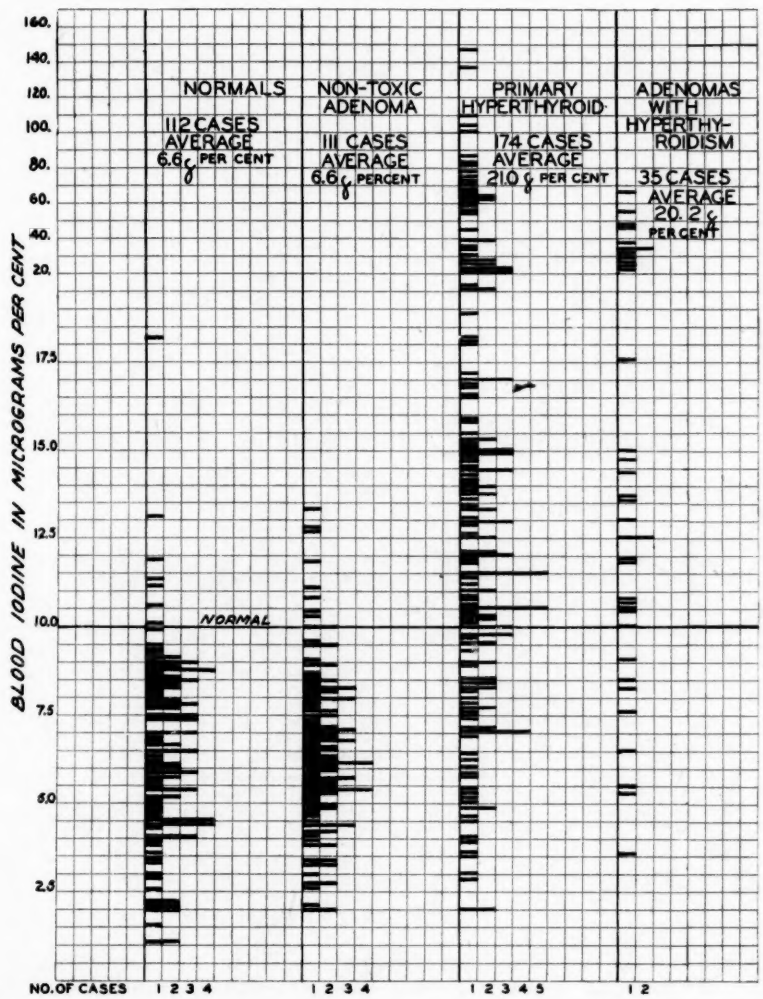
Biochemical investigation has done much to elucidate more clearly some of the physiological factors associated with thyroid disease. Of recent years, improved methods of quantitative blood iodine estimation have more firmly established the presence of an abnormal iodine metabolism associated with increased physiological activity of the thyroid gland. In clinical hyperthyroidism, there usually exists a decrease in the iodine of the thyroid gland concomitant with an increase of iodine in the blood and urine. In order to place the relationship of the blood iodine to thyroid disease on a firmer basis, the present study was undertaken.

The group of cases studied to date and recorded herewith, number four hundred and sixty-six. This group included blood iodine estimations on one hundred and twelve normal individuals, one hundred and eleven patients with adenomatous goitre and no clinical toxicity, one hundred and seventy-four patients with primary hyperthyroidism, thirty-five patients with adenomatous goitre and secondary hyperthyroidism and thirty-two patients checked three and in some instances, six months following subtotal thyroidectomy for hyperthyroidism. Patients having other conditions known to influence the blood iodine level such as gallbladder disease, elevated temperature or treatment with iodides for conditions other than thyroid disease, were not included. All other cases were included. Except in the group of normal individuals, the blood was secured from the patient in a fasting and basal state. The sex was not differentiated since we have not found any appreciable difference in blood iodine levels between men and women.

The method of blood iodine analysis developed by one of us (H. J. P.) and reported elsewhere[4] has been used with success to an error of less than ten per cent in over eight thousand analyses.

The blood iodine range on one hundred and twelve normal individuals varied from 1.1 to

CHART 1.

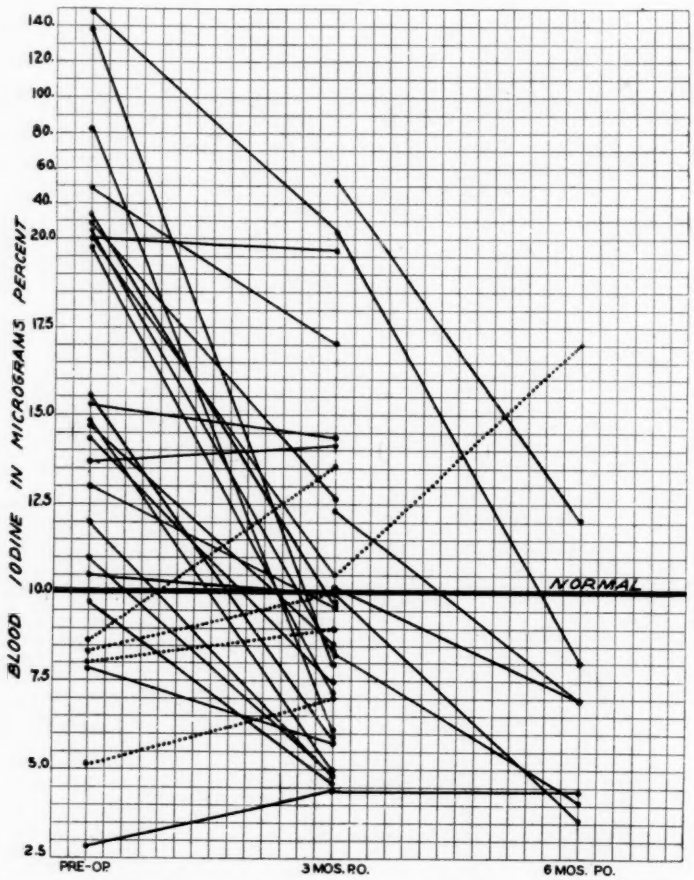


18.3 gamma per cent with an average of 6.6 gamma per cent. One gamma is synonymous with one microgram and is equivalent to .001 milligrams. Seven normal individuals had a blood iodine concentration in excess of ten gamma per cent. Two of these individuals were surgeons whose frequent contact with iodine might account for the increased blood concentration. One individual was of the nervous Latin race and temperament and consistently showed an elevated blood iodine concentration. The elevation of blood iodine in the other four cases could not be explained. Irrespective of this group we have tentatively adopted ten gamma per cent as the upper normal limit by our methods. (See chart 1.)

The blood iodine of one hundred and eleven clinically nontoxic adenomatous goitrous individuals was found to vary from 2.0 to 12.8 gamma per cent with an average of 6.6 gamma per cent. Of this group, there were eight cases in which a blood iodine concentration of 10 gamma per cent was exceeded. In four of these eight cases, although clinically the patients were nontoxic, the surgically removed thyroid showed secondary hyperplasia. In the remaining four cases there was no evidence of thyroid toxicity. (See chart 1.)

In one hundred and seventy-four cases of primary hyperthyroidism, the blood iodine range varied from 2.0 to 149 gamma per cent with an average of 21.0 gamma per cent. Of this group fifty-two cases or 30 per cent had a normal blood iodine in the presence of clinical and microscopical evidence of hyperthyroidism. Six of these fifty-two patients were in iodine remission but had no iodine therapy for at least one week prior to the test. While we are unable to satisfy ourselves as to the reason why 70 per cent of this entire group of cases should present an elevated blood iodine and 30 per cent a normal blood iodine, there are certain features of this latter group which have attracted our attention. In this 30 per cent group fall the more severe cases of the entire group in that they usually did not appear to respond so effectively to iodine therapy preoperatively, and as a result, two-stage operative procedures were

CHART 2.



Straight lines join blood iodine values of patients clinically improved.

Dotted lines join blood iodine values of patients with clinical recurrence.

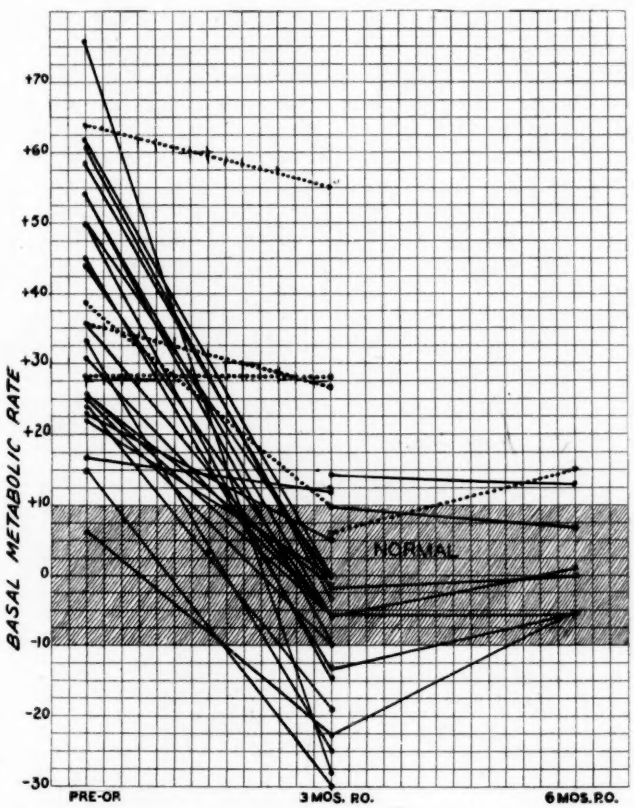
more often necessary. Such operative procedures were required in nineteen cases or 36.5 per cent of this latter group while, in all hyperthyroid patients passing through the Clinic, 22 per cent require two-stage operations. Primary hyperplasia with irregular involution of the excised thyroid was a consistent finding in patients from this group.

The blood iodine range of thirty-five individuals having adenomatous goitre associated with clinical toxicity varied from 3.6 to 66.5 gamma per cent with an average of 20.2 gamma per cent (chart 1). Of this group eight cases or 23 per cent had a normal blood iodine in the presence of clinical hyperthyroidism. Four of these eight cases were serious enough to warrant two-stage operative procedures.

In twenty-six patients who had subtotal thyroidectomy for hyperthyroidism, a striking decrease in blood iodine concentration, paralleling the decrease in basal metabolic rate, was found three months postoperatively in those cases where clinical improvement was present. The blood iodine relationship is shown graphically in chart 2 and the corresponding basal metabolic rates of the same patients in chart 3. Although three months after operation, the blood iodine in seven patients was still elevated above the upper normal limit, it was markedly decreased, relative to the preoperative blood iodine. Six patients had an elevated blood iodine three months postoperatively and four of these six cases had clinical evidence of persistent hyperthyroidism. (Dotted lines—charts 2 and 3.) All the cases of persistent hyperthyroidism were observed three months after their first operation, before which they had normal blood iodines. In view of this, we shall be interested to observe in further studies whether the tendency toward recurrence is consistently greater in those cases of clinical hyperthyroidism with a normal blood iodine.

A further decrease in blood iodine concentration was found six months postoperatively in seven cases, two of which had been followed since the preoperative period. One case (dotted line 3-6 months P O) had clinical evidence of recurrent hyperthyroidism at six months which was confirmed at the nine months checkup. The blood iodine (dotted line) was elevated at the six months' period preceding the patients' clinical manifestations of hyperthyroidism but de-

CHART 3.



Straight lines join B. M. R. values of patients clinically improved. Dotted lines join B. M. R. values of patients with clinical recurrence. Please note how drop in blood iodine in chart 2 parallels drop in basal metabolism in this chart.

creased to a normal blood level at the nine months' period when the presence of hyperthyroidism was evident. This one case reassures us of the real probability of a normal blood iodine in the presence of clinical hyperthyroidism and lends credence to the results of the hyperthyroid group shown in chart 1 with a normal blood iodine.

The presence of excess amounts of iodine in the blood of individuals with clinical hyperthyroidism has been reported by Dodds[5] and others[6, 7]. No reference, however, has been made to the possible presence of a normal blood iodine in hyperthyroid individuals except by Turner[8] and Perkin[9] who independently reported that 20-30 per cent of the cases studied by them had a normal blood iodine. This study confirms our former observations. These hyperthyroid patients with a normal blood iodine, as previously stated, did not appear to respond so effectively to preoperative Lugol's therapy; two-stage operative procedures were more frequently employed; and as suggested by the postoperative observations, the tendency toward persistent hyperthyroidism was greater.

We offer two possible explanations, based on clinical observations for the presence of a normal blood iodine in hyperthyroidism.

(a) In long-standing cases of hyperthyroidism which have not had iodine therapy, the thyroid gland becomes deficient in iodine as indicated histologically by the marked reduction of colloid material and chemically by iodine analysis[3]. In the earlier stages of the disease, there is an excess of iodine in the blood[6] and urine[10], the urinary iodine being a direct loss to the body. It is reasonable to assume, therefore, that a time would be arrived at when the thyroid could no longer sustain the excess iodine of the blood and urine and these values would then fall to a normal or even subnormal level. In support of this viewpoint is the fact that in the toxic adenomatous group, who had not had iodine therapy, there were no cases with a normal blood iodine. On such a hypothesis, the size of the thyroid gland at the initiation of hyperactivity would prolong the time that an elevated blood iodine could be maintained.

(b) Study of the remaining fifty cases of hyperthyroidism with a normal blood iodine revealed that they had all received repeated iodine treatment prior to hospitalization. The greater number of cases receiving therapeutic x-ray treatment for hyperthyroidism were also within this group. The increased severity of this clinical state has been pointed out above. This confirms the observation made by others[11, 12] that intermittent iodine therapy in hyperthyroidism may be a very unwise procedure.

The blood iodine studies on the group of patients before and after subtotal thyroidectomy for hyperthyroidism with clinical improvement in most cases and recurrence in a few, definitely illustrate, we believe, a relationship between clinical hyperthyroidism and the blood iodine level. It is not to be inferred that we believe iodine to be the sole factor in the etiology of thyroid disease but we do feel that it is a primary one.

Part III

An Iodine Tolerance Test

In view of the findings that single blood iodine estimations were not always capable of differentiating toxic and nontoxic goitre, we have, by frequent blood iodine estimations following the ingestion of a fixed dose of Lugol's solution, established the blood iodine curve in a given time period and called this the blood iodine tolerance curve. It is hoped that this test will be an objective criterion by which the presence of hyperplasia in the thyroid gland may be predicted in any particular patient.

The technique of the test may be reviewed briefly as follows: 10 cc. of blood is withdrawn from the patient, following which a known amount of iodine as Lugol's solution (37.5 milligrams iodine used at present) in milk is given orally. At one-half hour, one hour, one and one-half hours and at two and one-half hour periods, two cc. blood samples are taken. The morning of the test, no breakfast is given. All other meals are allowed. Iodine estimations are carried out on the separate samples of blood. The blood iodine curve with respect to time is graphically plotted.

The difference in blood iodine curves between the normal, nontoxic adenomatous and hyperthyroid individual is illustrated in chart 4.

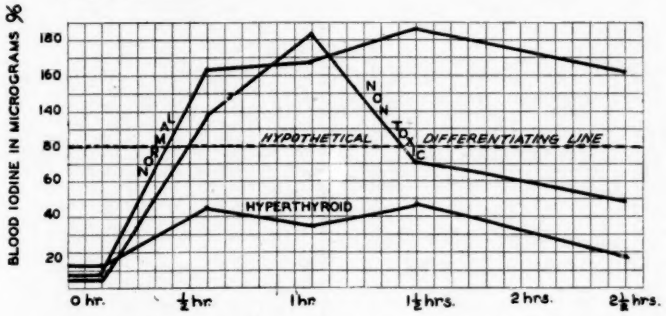
From the above chart it may be seen that the blood iodine curve does not rise to such a high level in the hyperthyroid individual as in the normal or nontoxic goitrous patient. It is reasonable to assume that a hypothetical line exists differentiating the normal and nontoxic goitre whose blood iodine curve rises above, and the individual with hyperthyroidism whose blood iodine curve falls below this line. This hypothetical line is tentatively placed at 80 gamma per cent in the above chart. Obviously, the height of the differentiating line would be dependent on the amount of iodine ingested and the differentiating principles obliterated when very large or very small doses of iodine were given. Thus an optimum dosage of iodine exists whereby the greatest variation between the normal and abnormal is obtained. Our work to date indicates that this optimum dosage varies in different geographical regions since 75 milligrams of iodine was differentiating at Toronto, Canada[9] while 37.5 milligrams appears to be closer to the optimum in this area. The relatively larger number of cases with nodular goitre in the Toronto area in contrast to the greater proportion of primary hyperthyroid

cases seen at the Lahey Clinic may account for this difference or there may be other variable factors which at present are not clear.

It would appear from our work to date, that the differentiating principle in these tests may be attributed to the degree of physiological and pathological activity of the thyroid gland. The work of Elmer[13, 14] lends support to such a hypothesis by his method of tracing the blood iodine curve and urinary excretion of iodine in myxedematous, normal and hyperthyroid individuals following the injection of 1300 gamma of iodine as potassium iodide. The blood iodine curves of four typical cases with thyroid enlargement are shown in chart 5. The level to which the blood iodine rises, dependent upon the pathological state of the thyroid gland, differentiates the toxic and the nontoxic goitrous individual. To date we have effected iodine tolerance tests on about sixty individuals and our results with a few idiosyncrasies are essentially the same as those reported.

CHART 4.

Graphs showing relationship of blood iodine concentration to time in normal, nontoxic goitrous, and hyperthyroid individuals following the oral ingestion of 6 min. of Lugol's solution 37 mgm. of iodine.



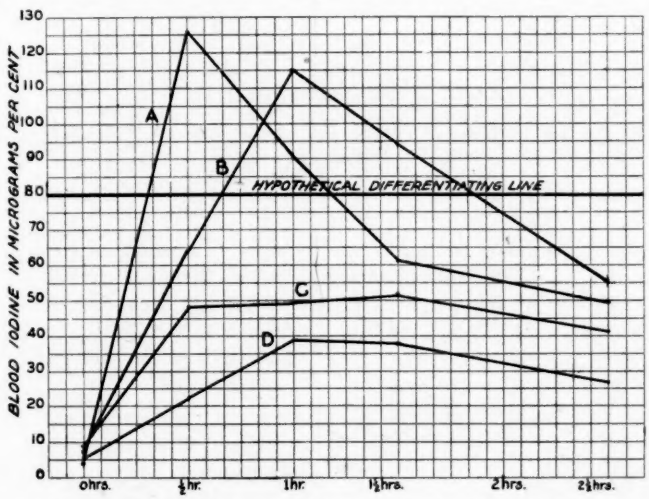
Normal—Male—Aged 35. B. M. R. —0. No clinical indication of thyroid abnormality.

Nontoxic goitre—Female—Aged 45. B. M. R. —9. Clinically nontoxic adenomatous goitre.

Hyperthyroid—Male—Aged 32. B. M. R. +83. Typical primary hyperthyroid—35 lbs. wt. loss.

Note the rejection of iodine as shown by elevation of blood iodine above the hypothetical line in normal and nontoxic goitres and the acceptance of blood iodine as shown in this chart in the case of hyperthyroidism.

CHART 5.



A. Miss M. B.—Aged 21. Adolescent colloid goitre. B. M. R. (+10) (—2).

B. Mrs. I. E.—Aged 45. Clinically and pathologically proved nontoxic adenomatous goitre. B. M. R. (—4).

C. Miss M. O.—Aged 24. Clinically and pathologically proved primary hyperthyroidism. B. M. R. (+70).

D. R. L.—Aged 22. Clinically and pathologically proved primary hyperthyroidism. B. M. R. (+53).

Note in C. and D. (toxic thyroids) the acceptance of iodine and in A. and B. (nontoxic goitres) its rejection.

These iodine tolerance curves are, however, subject to variation. At present they must be interpreted in the light of the clinical picture as a whole. Further study will clarify the irregularities that occur and make their correct interpretation more possible. It is hoped that the iodine tolerance test may prove diagnostically valuable in a manner similar to that which sugar tolerance curves have in diabetes.

SUMMARY

1. Some of the fundamental facts regarding iodine and thyroid secretion are discussed.
2. Blood iodine ranges have been established on normals, nontoxic adenomatous goitrous and hyperthyroid individuals in the New England area.
3. The presence of an elevated blood iodine in all cases of clinical hyperthyroidism is not absolute. Twenty-nine per cent had a normal blood iodine.
4. An elevated blood iodine in hyperthyroidism appears to be compensatory and desirable; if not present it at least suggests an intense state of thyroid intoxication.
5. Following subtotal thyroidectomy for hyperthyroidism, when clinical improvement is present, the blood iodine is decreased in relation to the preoperative blood-iodine, and elevated when persistent or recurrent toxicity is present, although in extreme cases, it may remain unaffected by the surgical procedure.
6. An iodine tolerance test is described which may prove to be a valuable asset in establishing a diagnosis of hyperthyroidism.

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MORTALITY FACTORS IN ACUTE APPENDICITIS*

Study of 1,000 Cases

BY EDWARD D. LEONARD, M.D., † AND SIDNEY DEROW, M.D.†

ONE thousand consecutive cases of acute appendicitis operated upon at the Newton Hospital have been studied in an effort to determine the possible factors influencing the mortality rate. Fourteen hundred and two cases (1923-1933) reported as clinical acute appendicitis were reviewed. Four hundred and two of this number, although presenting clinical pictures of acute appendicitis, were not included in this series, because of the pathological reports which did not confirm this diagnosis. The remaining 1,000 cases were positive acute appendices and their complications. There were forty-seven deaths in this group giving a mortality rate of 4.7 per cent.

The factors which appear to affect the mortality rate are individually discussed below.

Sex. Five hundred and forty of the patients were males and four hundred and sixty were females. The former group accounted for twenty-five deaths (4.6 per cent) and the latter group for twenty-two deaths (4.8 per cent). The disease was more prevalent in males, but the difference in the mortality rates between the two was negligible.

Age. As the accompanying graph (chart 1) illustrates, the condition is most common in the second and third decades of life (57 per cent of all the cases fall in this period). Fortunately, the mortality rate is lowest (2 per cent) in these cases (see chart 2). The death rate during the first five years of life is relatively high (8 per cent). Beginning with the end of the fourth decade there is a steady rise in the mortality rate. The percentage of perforated cases (chart 3) in the different age groups runs a course parallel to the death rate. Seventy-four per cent of all the patients under five years of age in this series showed free pus at the time of operation. Fifty per cent of the cases over fifty years of age had peritonitis or abscess formation. The above findings emphasize the importance of early diagnosis and operation in these age groups.

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Duration. Charts 4 and 5 illustrate vividly the relationship of duration of the disease before operation to the mortality. Eighty-four cases of acute appendicitis, five of which had peritonitis, were operated upon within ten hours after the onset of the symptoms without a single death. Following this relatively safe period, the mortality rate after operation increases steadily reaching a peak (13.9 per cent) on the fourth and fifth days after the onset of symptoms. Operation done after this period shows a slight but definite drop in the mortality rate. The death rate on the fourth and fifth days without doubt places this period in that group of

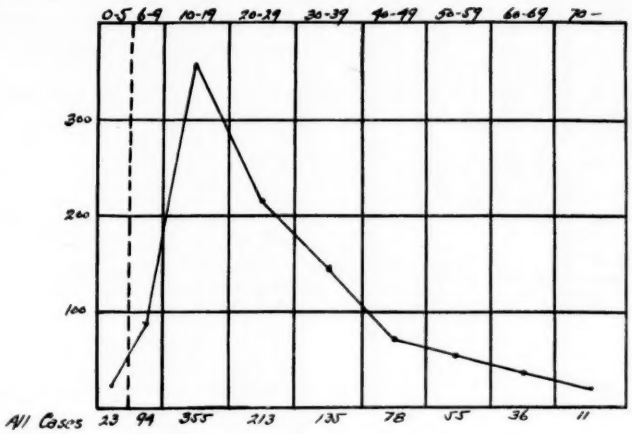

CHART 1. Age Incidence in All Cases.

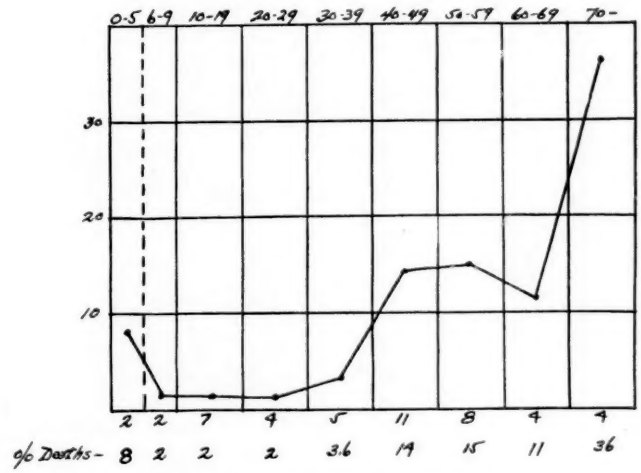

CHART 2. Age Incidence in Mortality.

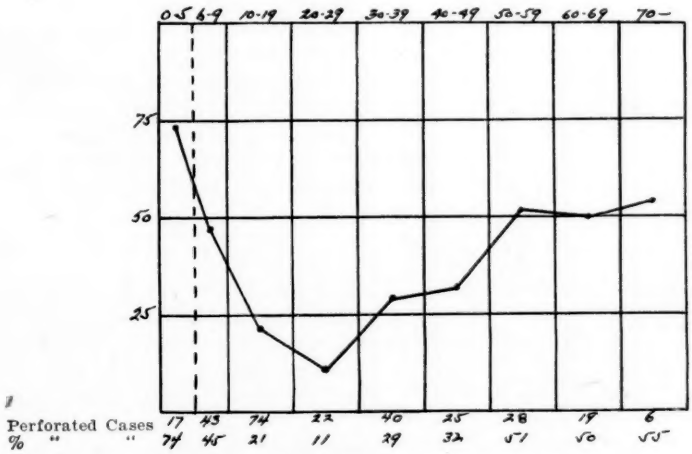

CHART 3. Age Incidence in Perforated Cases.

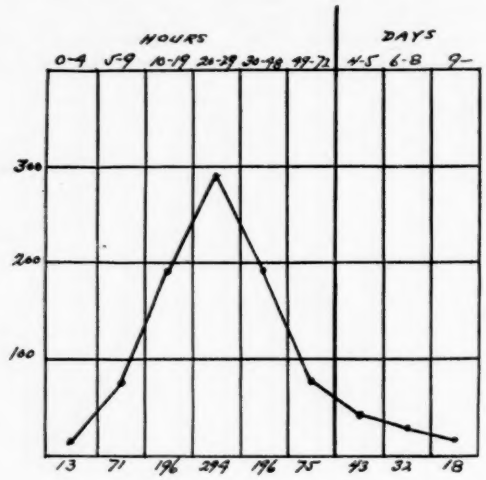

CHART 4. Duration and Incidence.

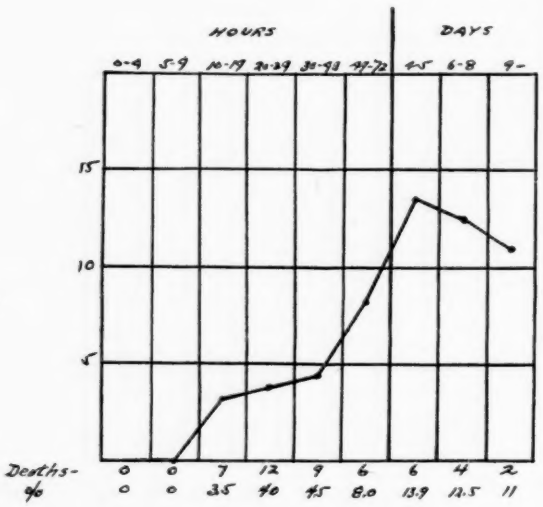

CHART 5. Duration and Mortality.

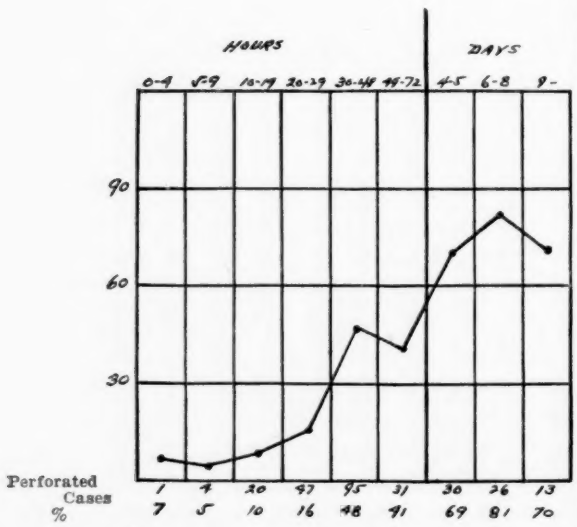

CHART 6. Duration and Perforation.

cases which are "too late for early surgery and too early for late surgery". Findings similar to these have been discussed by Walker, Coller and others. The percentage of cases of perforation varies directly with the duration of the symptoms before operation (chart 6).

CATHARSIS

	All Cases (1,000)	Perforated Cases (274)	Deaths (47)
History of Catharsis	103	50	7
Per cent of Patients who took Cathartic	10.3	18	15

Forty-eight per cent of all the patients who gave a history of catharsis had ruptured appendices at operation. Fifteen per cent of all the deaths were patients who took cathartics. These figures show another strong influence on the death rate before the patient actually comes to operation. It is therefore apparent that operation in itself will never lower the death rate sufficiently until the laity is taught not to treat all "stomach aches" with cathartics and waiting for symptoms to cease.

PREVIOUS ATTACKS

	All Cases (1,000)	Perforated Cases (274)	Deaths (47)
History of Previous Attacks	234	42	5
Per cent of Patients having Previous Attacks	23.4	15	10.6

Conclusions have not been drawn from these figures because many past histories were brief. However, they do stimulate interest in future studies and show that one attack of appendicitis does not immunize against future attacks. A number of patients who died undoubtedly would be alive now if the appendix had been removed during the interval rather than to have waited for another acute attack. The quality of surgical service undoubtedly has a definite relation to mortality statistics in this disease.

ANESTHESIA

	No. of Cases	Deaths	Per Cent Deaths
Gas Oxygen Ether	961	40	4.1
Gas Oxygen	7	1	14.2
Spinal	25	5	20
Local	7	1	14.2

Throughout this entire series ether was the anesthetic of choice. Gas oxygen and local anesthesias were used in cases gravely ill at time of operation. Spinal anesthesia was employed in some elderly patients with pulmonary compli-

cations. There were two definite spinal deaths on the operating table. Gas oxygen ether anesthesia in itself was not the cause of any deaths in this series.

OPERATIVE PROCEDURES

a. *Incision.*

Type of Incision	No. of Cases	Deaths	Per Cent
Right Rectus	900	41	4.5
McBurney	65	2	3.0
Midline	34	4	11.9

One case presented as a strangulated hernia and the operation included the removal of an acute appendix through a right inguinal incision. The inadvisability of midline incisions for this condition is apparent; they were used in this series in a few cases presenting a question of diagnosis in a female. Although McBurney incisions were used in only sixty-five cases, the low death rate is worthy of note and future study. Reid has reported interesting results with the use of this incision. (At present the Service is running a series of McBurney incisions, since a comparison between the results of right rectus and McBurney incisions will be of instructive interest.)

b. *Drainage.*

Four hundred and eighty-six cases were drained and forty-three of the deaths were in this group. In recent years drainage in early spreading peritonitis has been instituted more infrequently than in the past. Many surgeons strongly advise against drainage in these early cases. In this series drains were used rather often. Except for possibly a more prolonged stay in the hospital, we do not feel that drainage in itself contributes very strongly to immediate mortality in acute appendicitis. It is, however, an important factor in postoperative late complications such as hernia and intestinal obstruction. Various writers have proved the inadequacy of drainage and we drain at present fewer cases than we did in the past. It is difficult to forget the old dictum "When in doubt, drain."

c. *Disposition of Appendix Stump.*

The stump was inverted in 582 cases. No relation between inversion of the stump and mortality could be ascertained.

The great majority of drainage cases showed peritonitis or abscess at operation. Appendectomy with appendicostomy or cecostomy was done in seven cases with no deaths; although this is a small collection of cases, it is of significance. Some writers advise routine appendicostomy or cecostomy in all cases of spreading peritonitis.

d. *Type of Operation.*

	Cases	Deaths
Appendectomy without Drainage	512	2
Appendectomy with Drainage	436	39
Incision and Drainage, Appendix not removed	40	2
Appendectomy with Drainage and Ileostomy	1	0
Appendectomy with Drainage and Cecostomy	6	0
Appendectomy with Drainage and Appendicostomy	1	0
Incision and Drainage and Ileostomy (Both patients moribund)	2	2

COMPLICATIONS OF ACUTE APPENDICITIS FOUND AT OPERATION

Complication	Patients	Deaths	Per Cent
General Peritonitis	132	25	19
Local Peritonitis	48	4	8
Appendix Abscess	82	5	6
Pelvic Abscess	4	1	25
Pelvic Peritonitis	8	1	12
Total	274	36	13.1

The death rate in acute nonruptured appendicitis was 1.5 per cent.

The case listed as a death from Pelvic Abscess was a woman seven months pregnant, who came into the hospital ten days after onset of symptoms. She was moribund and had intestinal obstruction. Her prognosis was hopeless from the beginning.

POSTOPERATIVE COMPLICATIONS IN PATIENTS DISCHARGED AS RECOVERED

Complications	Number of Patients
Scarlet Fever	1
Wound Sepsis	35
Fecal Fistula	5
Hematoma of Wound	1
Delayed Wound Healing	5
Paralytic Ileus (Intestinal Obstruction)	7
Acute Pharyngitis	2
Pelvic Abscess	10
Postoperative Hemorrhage	1
Retropharyngeal Abscess	1
Upper Respiratory Infection	3
Acute Bronchitis	3
Lobar Pneumonia	3
Bronchopneumonia	3
Hemolytic Streptococcus Septicemia	1
Phlebitis	1
B. Coli Bacteremia	1
Rheumatic Heart Disease	1
Pyelitis	2
Abdominal Wall Abscess	6
Acute Cystitis	1

SECONDARY OPERATIONS ON PATIENTS DISCHARGED AS RECOVERED

Complications	Number of Patients
Incision and Drainage Abdominal Wall Abscesses	9
Abdominal Drainage Pelvic Abscess	3
Rectal Drainage Pelvic Abscess	1
Vaginal Drainage Pelvic Abscess	1
Secondary Wound Suture	3
Ileostomy	8
Transfusion	3

CAUSES OF DEATH AS LISTED ON HOSPITAL RECORDS

Complications	Number of Patients
Peritonitis	29
Intestinal Obstruction	4
Paralytic Ileus	12
Acidosis	1
Pulmonary Embolus	6
Hemolytic Streptococcus Septicemia	2
Bronchopneumonia	1
Circulatory Failure (Old Age)	3
Spinal Deaths	2

SECONDARY OPERATIONS ON PATIENTS THAT DIED

Complications	Number of Patients
Enterostomy	6
Transfusion	1
Multiple Incision and Drainage of Abdominal Abscesses	1

CONCLUSIONS

Mortality, in the average cases of acute appendicitis, is not the result of a single factor, but is due to a combination of factors. Of prime significance in the causes of mortality are the following:

1. *Age* of the patient.
2. *Duration of Symptoms* before operation.
3. *Catharsis.*
4. Type of *Anesthesia.*
5. Type of *Operation.*
6. *Postoperative Care.*
7. *General Condition* of patient *before operation.*
8. *Skill and Judgment* of each individual *Surgeon.*

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SYMPTOMATIC PSYCHOSES WITH BROMIDE INTOXICATION*

Their Occurrence in Southern New England

BY PAUL WILLIAM PREU, M.D.,† JOHN ROMANO, M.D.,† AND WARREN T. BROWN, M.D.†

INTRODUCTION

CASES of bromide intoxication with symptomatic psychosis have been reported from Maryland by Wuth[1], Diethelm[2], and Wainwright[3]; a series from Colorado has been described by Wagner and Bunbury[4]; cases from Texas have been described by Harris and Hauser[5], from Pennsylvania by Levin[6], and from North Carolina by Craven[7]. In spite of the wide distribution and the obviously increasing recognition of this condition, cases have been seen with such frequency in New Haven that it seems justifiable to call to the attention of the physicians of New England certain dangers in the use of bromide, and to point out the specific methods for the diagnosis and treatment of bromidism.

Credit should be given to Wuth for awakening interest in bromide intoxication in this country. He devised a simple laboratory method for the quantitative estimation of bromide in the blood, which will be described below. Since the publication of his paper in 1927, knowledge of psychoses with bromide intoxication has been extended by other investigators, until at the present time this group of mental disorders is one of the best understood psychiatric conditions.

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PHARMACOLOGY

The principal action of bromide is its depressing effect upon the central nervous system. Because of this valuable sedative action it has been extensively employed in the treatment of nervous and mental diseases. Many consider it the most effective drug for the treatment of idiopathic epilepsy. It is a valuable aid in the management of tensional states accompanied by anxiety and insomnia. In suitable cases, if the patient remains under constant medical supervision, the use of bromide is safe. Bromide is readily absorbed from the stomach when given by mouth and appears in the urine within a few minutes after ingestion. The elimination of the drug from the body proceeds slowly however. Bromide tends to displace chloride in the blood and other body fluids, where it may accumulate to such an extent that a state of intoxication is produced. The chloride which is displaced is excreted by the kidney in preference to bromide[8]. The interchange of chloride and bromide apparently involves equilibrium reactions since the administration of large amounts of chloride accelerates the elimination of bromide. It follows that the danger of intoxication is diminished by a generous chloride intake, and is exaggerated in states of malnutrition, cachexia, and dehydration, in which the intake of fluids and chlorides may be limited, or the stores of these substances in the body depleted. Impairment of renal function in nephritic and arteriosclerotic conditions may also enhance the risk of intoxication.

SYMPTOMATOLOGY

If the accumulation of bromide in the blood and tissues continues, definite intoxication develops. Several authors recently have described the symptoms of bromide intoxication in detail with special reference to the psychiatric manifestations. Diethelm[2], Wainwright[3], and Levin[6], have published excellent descriptions of the clinical pictures they observed. The symptomatology will be reviewed here briefly in order to call attention to two points which are of special importance to the internist: first, the delirious or "symptomatic" character of the mental disturbances; and secondly, the apparent independence of the psychiatric and dermatologic symptoms of intoxication.

The early symptoms of bromide intoxication are an exaggeration of the therapeutic sedative effect. Definite retardation of thought, speech, and action appears, together with anorexia, constipation, weakness, and drowsiness. This stage of intoxication is seldom dangerous if it is recognized before the appearance of frank psychosis; and the symptoms clear up gradually when the administration of bromide is discontinued. If this is not done, however, and the drug continues to accumulate, outspoken psychosis, which may cause serious difficulty, frequently occurs. Drowsiness and lethargy may be replaced by insomnia and irritable restlessness. The patient refuses food and fluids and may become severely dehydrated. Dry mucous membranes, furred tongue, foul breath, dilated pupils, ataxia and tremulousness are typical symptoms of the more severe states of intoxication. Symptomatic or delirious psychotic manifestations appear.

A disturbance of consciousness, the characteristic feature of symptomatic psychosis[9], is manifested by the primary symptoms of delirium: disorientation, fluctuation of the level of awareness and disturbance of memory. These symptoms are directly dependent upon an organic disturbance of cerebral function. On the basis of this organic disturbance of the sensorium, the patient usually develops more elaborate secondary symptoms which are colored by constitutional and personality factors and by his way of experiencing the organic delirium. Delusional trends, hallucinations, and emotional disturbances are produced which complicate the clinical picture.

In some cases, for reasons which are not entirely understood, skin lesions appear. The eruption usually is pustular acneform in type, indistinguishable in appearance and distribution from acne vulgaris. These cutaneous eruptions generally appear only after prolonged administration of bromide[10], thus differing from the exanthems of drug idiosyncrasy. A preëxisting seborrheic tendency is said to predispose to bromide acne. No published studies of blood bromide with reference to the dermatologic lesions have been found; but it has been our experience that extensive skin eruptions may occur with relatively low blood bromide levels. Severe skin eruptions are found in the absence of psychosis; while the skin may be normal in the presence of outspoken mental disturbance. This point demands emphasis because some physicians prefer to wait for the appearance of a skin eruption before making a diagnosis of bromide intoxication. Dependence upon the bromide eruption as a diagnostic aid is one of the chief reasons why symptomatic psychoses due to bromide pass unrecognized. A blood bromide level of 250 mg. per cent or higher will account for a delirious psychosis in a patient who is in fairly good physical condition. Stated in another way: severe intoxication will usually be produced by a displacement of more than 30 per cent of the blood chloride by bromide. The delirious condition is due to the presence of bromide, however, not to the deficiency in chloride.

The existence of bromide intoxication is suggested, therefore, by psychiatric or dermatologic symptoms which may be found alone or in combination.

DIAGNOSIS

Most patients to whom bromide is given are suffering from some neuropsychiatric illness

which causes its own symptoms, so that if bromide delirium is superimposed a very complicated psychiatric picture is produced. If the characteristic symptoms of delirium are recognized, there is usually little difficulty in making the differential diagnosis; for disorientation, clouding of consciousness and memory defects cannot be attributed to a preëxisting mild neurologic or psychiatric condition or to a functional psychosis. If the bromide was given to allay the symptoms of an organic mental illness, such as psychosis with cerebral arteriosclerosis or delirium accompanying an infectious disease, the symptoms caused by bromide intoxication are sometimes indistinguishable from the symptoms of the original mental illness. Even in such cases, however, the presence of bromide intoxication may be suspected if there is a sudden exacerbation in the mental disturbance which is not accounted for by a change in the physical condition.

The skin lesions produced by bromide are not specific, but are of some diagnostic importance if a history of the administration of sedatives can be obtained, particularly if the eruption is associated with delirium.

A definite diagnosis of bromide intoxication can be made only by the identification of bromide in the blood or urine. Wuth's modification of the Walter-Hauptmann method is the standard laboratory test for bromide; and is sufficiently accurate for clinical purposes. Since the urine may be free of bromide when the blood bromide is high[11], the blood should always be examined. Either whole blood or serum may be used; the serum yielding lower readings, especially at low blood bromide levels. The test may be carried out readily in a small laboratory or physician's office. The blood protein is precipitated by trichloroacetic acid, the mixture is filtered and gold chloride added to the clear filtrate. A reddish brown color develops if bromide is present. The mixture is then compared with a standard in a colorimeter or by means of a comparometer.* The method is fully described by Wuth[1] and Diethelm[2]. It is well to determine the blood chloride simultaneously.

TREATMENT

The treatment of bromide intoxication consists of general supportive measures plus the administration of chloride to eliminate bromide from the tissues.

Since almost all the patients are admitted in a malnourished or dehydrated condition, steps should be taken to insure an adequate intake of food and fluid. It is our practice to give a high caloric soft diet rich in vitamins and a minimum of 4000 cc. of fluid a day to severely intoxicated patients. In psychotic cases feeding by gavage is frequently necessary. Repeated enemas should be given to combat the intestinal sluggishness.

Approximately ten grams of chloride a day should be given in addition to the salt contained in the ordinary diet. Except in emergency, parenteral saline is contraindicated, as Wile[11] has shown that the rapid elimination of bromide may cause damage to the kidney.

Chemical sedation is contraindicated and usually ineffective[7], although drugs are occasionally required to combat extreme excitement and noisiness. Continuous tubs and cold wet sheet packs are the best means of combating insomnia and excitement.

The intoxication can usually be controlled in less than three weeks by the methods described. The underlying illness, for which bromide was given, of course demands its own treatment.

CASE REPORTS

CASE 1. E. W., aged fifty-three, a single business woman, was admitted on February 12, 1934. Twenty years previously she had experienced a depression with complete recovery. The present illness had begun early in 1933 and had been characterized by increasing depression and agitation. Her family physician had administered an unknown quantity of bromide for several weeks before hospitalization in an attempt to quiet her. For a week before admission she had eaten poorly and had been increasingly drowsy.

On admission the vital signs were normal. There was a diffuse acneform eruption on the face and chest. The tendon reflexes were hyperactive. The patient was disoriented for time and place, showed fluctuation of the level of awareness and had auditory hallucinations. Her speech was slow, thick, and incoherent.

A soft diet was given, plus 3,000 cc. of fluid and eight grams of sodium chloride daily. Aften ten days the delirium subsided, revealing an agitated tensional depression. No further improvement in her condition occurred, and she was discharged against advice on March 26, 1935.

The serum bromide on February 12, 1934 was 125 mgm. per cent (15.5 mM/L*). On February 27, 1934 the serum bromide was not detectable.

Comment: Bromide was given in an attempt to manage an agitated depression in the home. A sedative effect was obtained; but the patient could not be fed properly, and within a few weeks became intoxicated.

CASE 2. M. M., aged thirty-five, a housewife, was admitted on December 21, 1934. Six years previously, following the birth of her first child, she had experienced a depression with complete recovery. A second child had been born in July, 1934; and a few weeks later she had again become retarded, depressed and hypochondriacal. At home, under the care of her family physician, she had eaten poorly and her mental condition had not improved. A suicidal attempt led to her admission to the Psychiatric Clinic.

On admission her physical status was not remarkable. Symptoms of a retarded depression were present; but there was no evidence of a symptomatic psychosis. She was discharged against advice, somewhat improved, on December 30, 1934.

*Manufactured by LaMotte Chemical Company, Baltimore, Md.

*Millimols per liter.

At home she became agitated; and on January 11, 1935, her family physician began the use of five grams of bromide daily in an attempt to quiet her. On January 18 she had hallucinations of giant Negroes armed with knives and of large dogs about to attack her. She struck at these imaginary enemies with household utensils. Her husband, who was with her constantly, maintained that she was always correctly oriented during the periods of hallucination.

She was readmitted on January 21, 1935. Her physical status again showed no abnormality. There was no skin eruption. She was retarded and depressed; but was correctly oriented and displayed no fluctuation of the level of awareness. There was no evidence of hallucinations in any of the sensory fields. When asked to recount her previous hallucinatory experiences, she said she had not been confused but had been frightened by the sudden appearance and disappearance of the hallucinatory images, which had seemed quite real to her.

No special treatment for bromide intoxication was given. Her depression did not improve, and she was again discharged against advice on March 9, 1935.

The serum bromide on readmission, January 11, 1935, was 200 mgm. per cent (25 mM/L). On January 27 the serum bromide was 75 mgm. per cent (9.3 mM/L); and on February 13 bromide was not detectable.

Comment: Although the patient was already eating poorly, bromide was given in an attempt to manage an agitated depression in the home. An intoxication quickly developed. The patient was not seen by a psychiatrist during the hallucinated period; but the history suggests a pure hallucinosis, not a delirium. Only three cases of bromide hallucinosis have previously been reported[6].

CASE 3. C. B., aged thirty-seven, a policeman, was admitted on January 19, 1935. He had been addicted to alcohol for over fifteen years. Early in December, 1934, after a prolonged alcoholic debauch during which little food was taken, an upper respiratory infection occurred, followed by a delirium with disorientation and visual hallucinations. He was restless, ate poorly, and attempts to quiet him with opiates and chloral hydrate were unsuccessful. He had been given six grams of bromide daily for eighteen days before admission to the Psychiatric Clinic.

On admission the vital signs were normal. He was markedly dehydrated and there was a diffuse acneform rash on the face and shoulders. Speech was slow and thick. A high caloric diet rich in vitamins was given with 5000 cc. of fluid and ten grams of sodium chloride daily. In four weeks the delirium subsided, and there was marked improvement in his physical condition. He was discharged on February 23, 1935.

On admission, January 19, 1935, 28 per cent of the total serum chloride was displaced by bromide. The serum bromide was 285 mgm. per cent (27.2 mM/L). On January 27 the serum bromide was 125 mgm. per cent (15.0 mM/L); and on February 12 serum bromide was not detectable.

Comment: Although the patient was already suffering from a toxic delirium and had been eating poorly, bromide was given in an attempt to control psychotic symptoms. Bromide intoxication quickly developed.

CASE 4. C. M., aged forty-nine, a widowed hairdresser, was admitted on March 7, 1935. In August, 1934, she had complained of fatigue, insomnia, palpitation, and "nervousness". She ate very poorly. She refused to consult a physician until February, 1935, and at that time refused hospitalization. Four grams of bromide were administered daily since February 14, 1935. After two weeks her speech became thick, and her actions, sluggish; and she became restless and hallucinated. She was then hospitalized for nine days with continued bromide medication. Her condition did not improve and she was transferred to the Psychiatric Clinic.

On admission the vital signs were normal. There was no skin eruption. A fine tremor of the outstretched hands and a suggestive bilateral lid lag were observed. A severe symptomatic psychosis was present with disorientation, fluctuation of the level of awareness, auditory hallucinations, and periodic attacks of low grade panic.

Elimination of the bromide was facilitated by hydration, and the administration of ten grams of sodium chloride daily. In two weeks the delirium subsided. Definite signs of thyrotoxicosis were then seen. The sleeping pulse rate varied between 100 to 120 per minute, and the basal metabolic rate varied from +25 to +35 per cent. After two weeks' administration of Lugol's solution, a subtotal thyroidectomy was done on April 9, 1935. The postoperative course was uneventful. The basal metabolic rate varied from —2 to +6 per cent, and the sleeping pulse rate was 70 to 90 per minute. Her symptoms improved slowly, and she was discharged on May 6, 1935.

On admission, 30.2 per cent of the serum chloride was displaced by bromide. The serum bromide was 225 mgm. per cent (28.1 mM/L). On March 16, 1935 serum bromide was 60 mgm. per cent (7.5 mM/L); and on March 25 serum bromide was not detectable.

Comment: Symptoms of thyrotoxicosis were not recognized. Although the patient was already eating poorly, bromide was given in an attempt to control supposedly functional symptoms. Intoxication quickly developed. The correct diagnosis of the underlying condition was possible only after the bromide had been eliminated.

CASE 5. S. K., aged forty-seven, a housewife, was admitted on March 25, 1935. About one year previously she had begun to complain of depression, retardation, and irritability. She resorted to drinking large quantities of alcoholic beverages, took little food, and after a few months developed a severe polyneuritis. She became bedridden, and several physicians considered her condition grave. The administration of bromide was begun on March 10, 1935, and she received approximately 120 grams of sodium bromide in two weeks.

On admission the patient was stuporous. The vital signs were normal. The tendon reflexes of the arms were hyperactive. Both legs showed diffuse muscular atrophy, absent tendon reflexes, and suggestive foot drop. There was a slight acneform rash on the face and back.

Eight grams of sodium chloride were given daily with a diet high in caloric and vitamin content. Fluids were forced. After a few days the stupor cleared; and disorientation, fluctuation of awareness, and hallucinations were observed. The delirium and the neuritis improved rapidly under treatment. After the delirium subsided an irritable hypomanic condition was left, which disappeared within a week.

On admission 48 per cent of the serum chloride was displaced by bromide. The serum bromide was 350 mgm. per cent (43.7 mM/L). On April 8, 1935 the serum bromide was 100 mgm. per cent (12.5 mM/L); and on April 18, the serum bromide was 50 mgm. per cent (6.25 mM/L).

Comment: Although the patient was already in a critically malnourished condition; and had an alcoholic avitaminotic neuritis, bromide was used in an attempt to quiet her. Severe intoxication quickly developed.

CASE 6. S. W., aged forty-one, a housewife, was admitted on April 6, 1935. Four years previously a diagnosis of parenchymatous neurosyphilis had been made and confirmed by cerebrospinal fluid serology, pleocytosis, and increased protein content. She had received no specific treatment. For the past six years she had complained of irregular periodic girdle pains which had been interpreted as "heart attacks". The pain always began suddenly, bore no relation to exertion, and was not associated with dyspnea. Opiates had relieved it. A number of weeks before admission, bromide had been prescribed in an attempt to relieve one of these attacks. The drug had been continued indefinitely and had been purchased in pint-size bottles. She became stuporous and ate very little food. No convulsions had occurred.

On admission the vital signs were normal. The pupils were fixed to light. There was no skin eruption. The blood Kahn was negative. The cerebrospinal fluid was under normal pressure and contained eight lymphocytes per c. mm. The Pandy reaction was strongly positive. The cerebrospinal fluid Wassermann was +4; and the colloidal gold curve was 4555555554.

A typical delirium was present with disorientation, fluctuation of awareness, and restlessness. The patient's general condition was poor, and parenteral saline was given to hasten the elimination of bromide. Because of extreme noisiness, morphine and hyoscine had to be given on several occasions. Her condition did not improve. She became stuporous, developed bronchopneumonia and died on April 24, 1935.

On admission the serum bromide was 350 mgm. per cent (43.7 mM/L). This was one week after bromide had been discontinued.

On April 2, 1935 the serum bromide was 150 mgm. per cent (18.7 mM/L).

Comment: Excessive quantities of bromide were given in an attempt to relieve attacks of tabetic pain. No attempt was made to control the chloride-bromide balance. A severe intoxication developed, and the patient died of an intercurrent bronchopneumonia before the intoxication could be controlled.

Postmortem examination of the brain: The gross appearance of the brain was entirely normal excepting the cerebral meninges, which appeared slightly thickened and cloudy. The Turnbull test for iron in the cerebral cortex was negative. Microscopic examination showed the cerebrospinal meninges infiltrated with small numbers of lymphocytes and plasma cells. This exudate was most marked in the meninges at the base of the brain and around the brain stem. There were none of the stigmata of general paresis. Sudan III and Weigert preparations of the spinal cord failed to reveal any evidence of tabes.

Throughout both occipital lobes were found numerous small patches of necrobiosis. These had a focal distribution and were limited to the cortical grey matter. None of the large pial or parenchymal vessels showed organic change. The cortical capillaries revealed marked endothelial swelling. Both temporal lobes showed a similar picture to a lesser extent. These changes resembled in all respects those found in functional vascular disease, having been described following epileptiform attacks.

CASE 7. A. M., aged twenty-four, a single man was admitted on April 21, 1935. Seven weeks previously he had fallen, striking his head and suffering concussion with hemorrhage from the mouth and right ear. He had been hospitalized, and had remained unconscious for five days. Roentgenograms of the skull were negative for fracture at that time. During the next few days he became restless and unmanageable. He was placed on a dehydration diet and six grams of bromide were administered daily in an effort to combat the posttraumatic excitement. He became stuporous; and then after three weeks became overactive, talkative, disoriented and hallucinated. On April 12, 1935 he was discharged from the hospital unimproved, with instructions to his family to continue the administration of three grams of bromide daily. At home he continued confused and restless, and admission to the Psychiatric Clinic was advised.

On admission the vital signs were normal. Severe dehydration was present. There was a diffuse acneform rash on the face and back. Neurologic examination was negative except for a right lower facial weakness. The cerebrospinal fluid pressure, color, protein and cell content were normal. The cerebrospinal fluid Wassermann was negative. A typical symptomatic psychosis was present with fluctuation of awareness, disorientation, confabulation, visual hallucinations, and restlessness. Speech was thick and slurred.

He was given ten grams of sodium chloride daily and a diet high in caloric and vitamin content. Fluids were forced. Wet sheet packs were used for sedation. In four weeks the delirium subsided, and his general physical condition showed great improvement, although the right facial weakness persisted. He was discharged on May 19, 1935 with instructions to return to the Neurologic Outpatient Clinic.

On admission 47 per cent of the total serum chloride was displaced by bromide. The serum bromide was 350 mgm. per cent (43.7 mM/L). On May 6, 1935 the serum bromide was 200 mgm. per cent (25 mM/L); and on May 13, 1935, the serum bromide was 60 mgm. per cent (6.25 mM/L).

Comment: Bromide was given in an attempt to control a posttraumatic delirium; and the patient was simultaneously given a dehydrating diet. Severe intoxication quickly developed. Hydrotherapy produced an excellent sedative effect.

CASE 8. S. H., aged thirty-one, a single man, was admitted on May 8, 1935. He had had petit mal attacks since fourteen and grand mal attacks since twenty-eight years of age. Phenobarbital and a low protein diet had been administered in an attempt to control the convulsive state. During March and April, 1935, the attacks had become more fre-

quent, and five grams of bromide had been administered daily. After about ten days of bromide treatment, he had become sluggish in speech and action. On April 28, 1935 a consultant diagnosed his condition as an organic psychosis and advised withdrawal of the drug. At that time the serum bromide was 300 mgm. per cent (37.5 mM/L). Fluids were forced and sodium chloride was administered, but the patient remained sluggish. Admission to the Psychiatric Clinic was suggested.

On admission the vital signs were normal. There was a diffuse chronic acne vulgaris on the face, shoulders, and back that had recently become more severe. No other physical abnormalities were noted. No evidence of delirium was observed, but there was definite mental sluggishness.

After ten days of hydration and increased sodium chloride intake, the sluggishness disappeared. The patient then had a major convulsive attack and was given phenobarbital daily. He was discharged on May 18, 1935 with instructions to continue the use of phenobarbital.

On admission 30 per cent of the serum chloride was displaced by bromide. The serum bromide was 225 mgm. per cent (28.1 mM/L). On May 11, 1935 the serum bromide was 75 mgm. per cent (9.3 mM/L).

Comment: Large amounts of bromide were given in an attempt to prevent epileptic convulsions, without any attempt to control the chloride-bromide balance. Moderate intoxication quickly developed, which fortunately was recognized before it became severe.

Case 9. H. H., aged sixty-three, a widowed housewife, was admitted on May 27, 1935. For five years she had complained of attacks of precordial pain radiating to the left arm, sometimes associated with dyspnea and pulmonary edema. During the past two years these attacks had become more frequent, and the patient had become more garrulous, circumstantial, and irritable. In February, 1935, she was hospitalized; and a diagnosis of general, coronary and cerebral arteriosclerosis was made. A diet low in fluid and sodium chloride was ordered. In May, 1935 after an anginal attack, bromide was prescribed, and she received seventy-five grams of the drug in two weeks. On May 16, 1935 she complained of poor vision, and in a few days became confused, disoriented, and hallucinated.

On admission the vital signs were normal. The tendon reflexes were hyperactive. There was a slight acneform rash on the back. Disorientation, fluctuation of awareness, and visual and auditory hallucinations were present.

She was digitalized, fluids were forced, and she was given eight grams of sodium chloride daily. The delirium subsided after three weeks, her general condition improved, and she was discharged on June 24, 1935.

On admission the serum bromide was 300 mgm. per cent (37.5 mM/L). On May 31, 1935 the serum bromide was 175 mgm. per cent (21.9 mM/L). On June 11, 1935, the serum bromide was 50 mgm. per cent (6.25 mM/L).

Comment: Bromide was given, in an attempt to control anginal pain, to an arteriosclerotic patient who was already on a restricted fluid and chloride intake. Severe intoxication quickly developed.

DISCUSSION

Cases of bromide intoxication with symptomatic psychosis have been seen surprisingly frequently in southern Connecticut. Two and seven tenths per cent of the patients admitted to the Psychiatric Clinic at New Haven Hospital during the past year have shown signs of definite intoxication with bromide. The nine cases reported here illustrate various aspects of the clinical problem.

The administration of bromide is clearly indicated only in the treatment of certain patients with organic convulsive diseases. Notkin[12] has shown that fairly large amounts of bromide may safely be administered indefinitely to epileptics if the chloride-bromide balance is carefully controlled, and if occasional determinations of the blood bromide content are made. Bromide, in doses of one to two grams a day, is sometimes useful in the management of mild nervous and mental symptoms, although in most cases a rapidly acting barbiturate, such as sodium amytal, is more effective. In the presence of renal damage, however, barbiturates are more dangerous than bromide. It must be kept clearly in mind that bromide must not be administered over any prolonged period unless an adequate intake of fluids and chloride is maintained; and the physician should be constantly alert for symptoms of bromide intoxication.

Bromide should not be employed in states of severe excitement and agitation because it is not effective unless dangerously large doses are given. Paraldehyde is not only more effective but is much safer in such states. Bromide should never be used in cases of delirium due to either toxic or infectious causes. It should be used with caution in cases of arteriosclerosis, since delirium is readily produced if cerebral arteriosclerosis is present. Nephritis is a definite contraindication to the use of the drug.

Bromide should not be used in cases of dehydration or severe malnutrition, in which the body fluids and chlorides are low.

In eight of the nine cases reported, deficient diet and dehydration seemed to play a definite rôle in the development of bromide intoxication. This fact has not been sufficiently emphasized in the literature.

An inadequate intake of fluids and chloride would seem as important a factor in producing bromide intoxication as the actual amount of bromide taken. The experience of Notkin[12] with epileptics illustrates this point clearly.

The skin eruption is not a reliable criterion of bromide intoxication. The question of bromide exanthems will be discussed in greater detail in a subsequent paper. A skin eruption was present in six of the nine cases in our series; but in no case was it considered severe enough to be in itself an indication for treatment.

The management of psychiatric illnesses in the community is no simple problem. Sedatives are often necessary; and the patient or his family may refuse to consider hospitalization. The attending physician has to make the best of the situation.

More general appreciation of the importance of the recent studies of bromide intoxication, however, will facilitate the successful management of such cases.

SUMMARY

1. Nine cases of bromide intoxication with symptomatic psychosis are reported.
2. The pharmacology of bromide is summarized; and the symptomatology, diagnosis, and treatment of bromide intoxication are briefly reviewed.
3. The frequency of bromide intoxication in southern New England is noted.
4. Reasons for the occurrence of bromide intoxication are advanced, and suggestions for its prevention are offered.

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AN ANALYSIS OF THREE HUNDRED CASES OF ASTHMA IN CHILDREN*

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THE bulk of the work upon asthma deals with groups composed either solely or in a large part of adults. The problem of asthma among children is sufficiently different to warrant its separate consideration. This series is

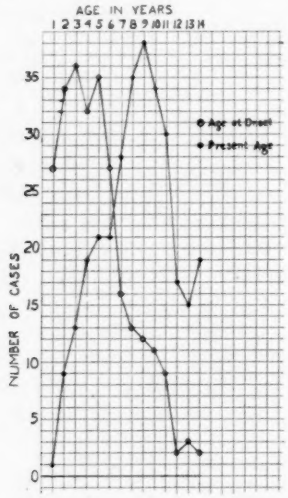

CHART 1. The Age at Onset of 300 Cases of Asthma in Children.

composed of 300 children, under fourteen years of age, who have been seen by me at the Massachusetts General Hospital during the last three years. The average age of the patients at the time of examination was seven years and nine months.

Between twenty and fifty protein tests were done upon each child, the common food, animal and pollen allergens being used. The scratch test was most commonly employed, although in the last year, many of the pollen and animal emanation tests were done by the intradermal method as well. The combined methods gave a much higher percentage of positive tests in pollen disease than we had secured by using the scratch test alone[1].

The age of the onset of asthma was first considered and is shown in graphic form in the accompanying chart. The exact time of onset is often difficult to determine with any degree of accuracy since the early attacks are frequently mistaken for respiratory infections. However, one case in the series began as early as the second month, two in the third month, one in the fourth, and one in the fifth month. Cases having their onset after the sixth month were not infrequent. About 10 per cent had their onset in the first year, and 12 per cent in the second year. Sixty-six per cent began during the first six years. After the sixth year a sharp drop occurred in the incidence of new cases. The average age of onset for the entire group was 4.6 years.

Results not markedly at variance with these figures were reported by Chobot and by Peshkin. Chobot[2] in a series of 100 children found that 10 per cent of the cases had their onset in the first year and 19 per cent in the second year. Peshkin[3], in a group of 100 children, states that he found the commonest age of onset to be the second year.

There is a general impression that an allergic

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family tendency influences the time of onset of asthma. A series of adults reported by Spain and Cooke[4] showed the average age of onset for patients with a positive family history to be twenty-five years. Those having a negative family history had an average age of onset of thirty-five years. The allergic families developed asthma much earlier than did the nonallergic families. These authors included under the heading of a positive family history those cases having a positive collateral family history as well as those having a direct family history of asthma or hay fever. Using these limitations they found that 58.4 per cent of their series of 462 cases had a positive antecedent family history. Moreover they ascertained, in a group of 115 normal individuals, that only 7 per cent had such a positive history. In 52.9 per cent of thirty-four cases having a bilateral family history the onset of symptoms occurred in the first five years of life and in 26.4 per cent the onset occurred in the second five years of life.

In our children's series, no such difference was found between these two groups. Children with a positive family history showed an average age of onset of 4.3 years, while the children having a negative family history showed an average age of 4.4 years. The group showing a positive family history, either of direct or collateral inheritance, was further analyzed. Twelve cases had a bilateral inheritance. In this group the average age of onset was 4.7 years. Fifty-eight cases having a unilateral inheritance showed an average age of onset of 4.1 years. As noted above, the group of 172 cases having a negative family history showed an average age of onset of 4.3 years. So it is seen that there is shown no significant difference in the age of onset of asthma in children whether the family history is negative or positive.

The influence of an allergic family tendency upon the occurrence of complicating allergic conditions was noted, also its influence upon the incidence of sensitization to more than one group of allergens. Of the total 300 cases, 38 per cent showed a positive allergic family history, and of these, 28 per cent showed eczema, hay fever, or other allergic conditions complicating the asthma. Of those having a negative family history, 23 per cent showed allergic conditions complicating the asthma. Individuals from the allergic families were apparently somewhat more prone to the development of complicating allergic conditions.

The question of multiple sensitization in relation to the family history is pertinent. Of the children with a positive family history, 30 per cent showed multiple sensitization. The nonallergic family group showed that 34 per cent of their number were sensitive to more than one of the four groups of allergens, which would indicate that the allergic family tendency is not a factor of importance in this connection.

Children with allergic heredity are more apt to develop allergic diseases than are children with a normal heredity, according to Balyeat[5]. Such children do not, however, show any great difference from the nonallergic group in the age of onset of their asthma, nor in the frequency with which they manifest multiple sensitization.

An analysis of the cases from allergic families showed that one or both parents were allergic in 40 per cent of the group; in 37 per cent the grandparents had been allergic; in 16 per cent the brothers or sisters were allergic. Of 178 cases in this group, the relatives showed asthma in 53 per cent of the cases, hay fever in 26 per cent, eczema in 13 per cent, urticaria in 1½ per cent, migraine in 1½ per cent, and vasomotor rhinitis in 1 per cent. There seems to be a marked tendency for families to show the same allergic condition in succeeding generations, viz., asthmatic parents transmit a tendency toward asthma rather than toward one of the other allergic conditions.

The question arises as to whether the early onset of asthma has any significance in forecasting the occurrence of complicating allergic diseases. Will the patient who shows asthma in the early years be more apt to develop hay fever, for instance, than the child whose asthma appears later in childhood? A tabulation showed that there were 214 cases of asthma which were uncomplicated by other allergic conditions, and that there were 86 which were so complicated. The first group showed an average age of onset of 4.1 years, the second group showed an average age of onset of 3.2 years. This would seem to indicate that the earlier the asthma manifests itself the more likely the patient is to develop complicating allergic conditions.

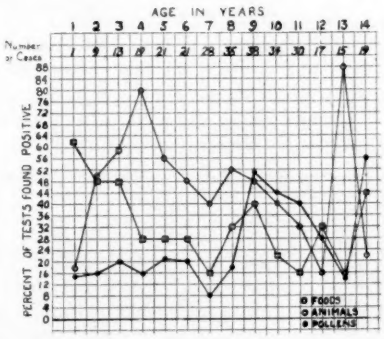

CHART 2. The Relative Importance of the Common Allergens at the Various Ages.

The importance of the various groups of allergens at different ages is an interesting study. This is graphically shown in Chart 2. This chart shows foods and animal emanations to be of about equal importance during the second

year; pollens to be of but little importance, comparatively. From the second year on, for several years, the animal emanations become more important and the foods less important. Pollens remain comparatively unimportant until the ninth year, when they are found to show the highest percentage of positive tests. All the allergens show a peak during the eighth and ninth years, and again during the thirteenth and fourteenth years.

It is obviously desirable to limit as much as possible the number of protein tests when dealing with children. With this object in view, an analysis of the tests was made. Of the many food allergens for which tests were made, a small group appeared to be of primary importance. There were 155 positive tests for foods. Of these, 21 per cent were for egg, 18 per cent for wheat, 9 per cent for milk, and 6 per cent for potato. The four foods just mentioned account for 54 per cent of the 155 positive tests for foods. The remaining 46 per cent of the group was divided among the common fruits, vegetables, meats, nuts, and cereals, other than wheat. Not one of the foods in this latter group was found positive in over 1 per cent of the total positive tests. Turning to the group of animal emanations we find 257 positive tests; of these 31 per cent were due to cat, 24 per cent to dog, 18 per cent to horse, 15 per cent to chicken feathers, 6 per cent to goose feathers. Cattle hair, rabbit hair, parrot feathers, wool and duck feathers occurred occasionally. The pollens gave a total of 256 positive tests. Of these tests, 30 per cent were due to ragweed, 18 per cent to timothy, 17 per cent to orchard grass, 16 per cent to red top, 7 per cent to cocklebur, 6 per cent to plantain. Other pollens were included in the tests but none accounted for more than 1 per cent of the series. House dust was frequently found positive. Its clinical significance is difficult to determine. Orris powder occurred occasionally.

Of the entire 300 cases, 67 per cent were found positive to one or more allergens, 47 per cent to animal emanations, 29 per cent to pollens, 25 per cent to foods, and 5 per cent to miscellaneous factors. Comparing these figures with those reported by Rackemann[6], for a group composed mainly of adult patients, we find that animal emanations and foods play a much less important rôle than is the case among the children.

The accompanying table shows the comparative importance of the four great groups of allergens in children and in adults. Many of the cases, of course, showed sensitivity to one or more of these groups.

A consideration of table 1 shows the foods and the animal emanations much less frequently positive among adults than is the case among the children. It seems fair to say that this is in most instances to be attributed to natural desensitization. It indicates a better prognosis among children for the recovery from asthma due to either of these two factors than is the case in the pollen asthma, which shows as high a percentage of positive tests in the adult group as occurs in the children's groups.

TABLE 1

	Rackemann Adult Group 924 Cases	O'Keefe Children's Group 300 Cases
Positive tests	46%	67%
Animal emanations	17%	47%
Pollens	33%	29%
Foods	7%	25%
Miscellaneous	5%	5%
Negative	54%	33%

The group reported by Rackemann is composed mainly of adults. It contains 425 cases classified as extrinsic asthma and 499 cases classified as intrinsic asthma. In the extrinsic group, positive tests were found in 82 per cent of the cases; in the intrinsic group the percentage was 17. The average of these two groups as shown in our table is 46 per cent. The children's group, in table 1, is composed of extrinsic and intrinsic asthma, and shows that 67 per cent of the cases exhibited positive tests.

CONCLUSIONS

About 10 per cent of the cases of asthma in children have their onset in the first year of life; 66 per cent have their onset during the first six years.

A positive family history of allergic disease does not influence the age of onset of asthma in children, or the frequency of multiple sensitization. Individuals from allergic families are, however, somewhat more prone to the development of complicating allergic conditions than are children from nonallergic families. As originally pointed out by Adkinson[7], there is a definite tendency to show the same allergic condition in succeeding generations.

In the first year of life the foods show the highest percentage of positive skin tests. In the second year, however, and after that, the animal emanations become of chief importance, until the ninth year when they are surpassed by the pollen antigens. In the thirteenth and fourteenth years the percentage of positive tests for all the antigens shows a very marked and sudden increase. This is especially true for the animal emanations. The onset of puberty may, in some way, be responsible for this sudden change.

The most important allergens concerned in the asthma of children are as follows:

Foods	Animal Emanations	Pollens	Miscellaneous
egg	cat	ragweed	orris powder
wheat	dog	timothy	house dust
milk	horse	orchard grass	
potato	chicken feather	red top	
	goose feather	cocklebur	
		plantain	

From this group of seventeen allergens the examiner will usually obtain information as to which group or groups should be more intensively investigated.

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MEDICAL PROGRESS

PROGRESS IN DERMATOLOGY, 1935

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ALLERGY

SOME years ago a physician in a suburb of Boston was heard to declare that syphilis had now become a routine affair. If the Wassermann is positive, the diagnosis is syphilis. If the diagnosis is syphilis you give arsphenamin. And that is all there is to syphilis nowadays. It would almost seem that a similar situation is developing in regard to allergy and the food tests, if one judges by the literature. Many physicians seem to believe that if one has to deal with a skin eruption the food skin tests will absolutely reveal both diagnosis and treatment. You test the skin with various sorts of food. If you get a reaction, the eruption is allergic. If the eruption is allergic, you take away the foods which caused a reaction and the patient gets well. That's all there is to allergic eruptions.

The editorial writer in the *New England Journal of Medicine*[1] does not think the matter quite so simple as that. He has this to say about the allergic skin tests: "It would seem that promiscuous skin testing should become a thing of the past. Proper selection of patient and test should be made in order to gain the proper scientific data and not subject the patient to unnecessary tests and expense. At the same time thought should be given to the variations in tests from time to time. Their evaluation demands experience and common sense."

Colmes[2] is even more specific and emphatic. He opens his article by saying, "That the diagnostic import of the protein skin test is not infallible and that frequent irregularities exist in the relationship between the skin reacting allergen and the patient's symptoms, has been recognized since the early studies on human hypersensitiveness." In confirmation of that statement Colmes quotes a number of authors; Blackfan who has seen an "egg" eczema with a negative egg test; Walker, who found that positive skin tests cannot always be incriminated as causative of the patient's symptoms; Schloss, who had the same experience as Walker; also Kern, Maytum, Rackemann, Feinberg, Stevens, Rowe, and Hill. Surely men of such repute would lend credence to any statement. After giving the tables of the results of his own studies Colmes concludes, "These results indicate that, in the study of allergic diseases, the positive skin reaction cannot be accepted as the sole basis for determining the offending factor."

Rackemann[3] at a recent symposium on allergy pointed out the increasing importance of the history and the decreasing significance of the skin test. A "good allergen" gives a typical wheal in a few cases and a negative reaction in most cases of routine testing.

Schmidt[4] brings out another point in regard to evaluating skin tests. He states that the various regions of the body do not react alike. The back reacts more strongly than the upper arm, the flexor surfaces than the extensor, the upper arm than the forearm. Hence in comparing results, one must make sure that all tests were made on the same region of the body. For instance, one should not compare a test made on the back with one made on the forearm. As to the back itself, Schmidt reports that wheals induced four fingerbreadths below the spine of the scapula were only half as large as those produced in the region of the spine of the scapula itself.

Urbach[5] has worked out a theory to explain why the allergic tests respond in one region and do not in another. The foundation of every clinical manifestation of an allergic disorder, he says, is an antigen-antibody reaction. In the main, the important factor in the manifestation

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of the allergic reaction is the location of the cellular antibodies. The antigen is far less important. He classifies the allergies on the basis of the site of the antigen-antibody reaction. This method, he claims, explains why only a test which is performed on the shock organ can give information concerning the type and degree of "allergization" of the involved tissue. Furthermore, by identifying the shock organ a more effective therapy becomes possible, for only that desensitization is effective which considers the primary point of attack (the epidermal tissue, the vasculocutaneous, the epimucobronchial, etc.) and that is applied to the involved organ (the epidermis, cutaneous vessels, bronchial mucous membrane, bronchial musculature, etc.). With few exceptions the clinical manifestations of an allergy are almost entirely determined by the organ in which the antigen-antibody reaction takes place. Eczema is one of the diseases in which the site of the primary attack is in dispute. Kryle accuses the epithelium but Jadassohn believes that a purely epithelial hypersensitivity is unlikely without a simultaneous involvement of the vascular system. Jadassohn, therefore, assumes a vascular epithelial origin. Urbach thinks that the primary site may be epithelial as well as vascular. He would explain the fact that a primary epithelial hypersensitivity may later be elicited by way of the vascular system on the basis of recent histologic studies. These indicate, he writes, that the reticulohistionic elements of the epidermis (the so-called Langerhans cells) and those of the cutis (the capillary endothelials of the papillary blood and lymph vessels) form a connected system, the Langerhans endothelial system. He maintains that a differentiation of a primary epithelial attack and a primary vascular attack can be made by pharmacological methods.

Oelgoetz, Oelgoetz and Wittekind[6] have also studied the mechanism of allergy. They, however, instead of talking about antigens and antibodies, as does Urbach[5], speak more of enzymes and pancreatic juices and the split proteins. They concern themselves in particular with foods and the gastrointestinal tract and, in general, with what happens *before* the food substances sensitize the organism. They give a summary of their observations on food behavior and their idea of a rational treatment based on their observations. Their summary is as follows: 1. Most of the protein ingested is not split up to the stage of amino-acids in the gastrointestinal tract. A large part of the protein is absorbed into the blood as acid or alkali-meta-protein and other derived proteins. The gastrointestinal tract is essentially a receiving and mixing mechanism. Digestion is started in the gastrointestinal tract but is continued and completed in the blood stream. 2. Normally, sufficient pancreatic juice is secreted to combine with all the food eaten and to provide for an excess which passes free (uncombined) into the blood stream where it acts as a buffer solution, combining with and digesting any food that has been absorbed unmixed with enzymes. 3. Blood serum normally contains free pancreatic enzymes in definite and constant concentration. These enzymes can be demonstrated. 4. The concentration of pancreatic enzymes in the blood stream of a person on a regular ration compared with that after taking a "test" meal, consisting quantitatively of a greatly increased total ration, appears to be a direct measure of that individual's pancreatic (digestive) function. 5. It is probable that hypersensitiveness to foods is caused by an excess of free food (food free of enzymes) in the blood serum and that this excess is caused by a low pancreatic threshold (hypofunction). 6. In the authors' opinion the state of allergy to foodstuffs can be determined by ascertaining the concentration of free amylase in the serum before and after a test meal. 7. The rational treatment of sensitization to foods lies in the reduction of the total food intake. If the patient can maintain normal weight and adequate buffer enzymes on the reduced ration, no other treatment is necessary. If he is unable to do so it would seem that dry pancreatic enzymes must be administered to make up the shortage.

Bearing in mind Urbach's statements that allergy is due to a cellular antigen-antibody plus reaction and that it is the antibody which is at fault rather than the antigen, Harley's conception of bacterial sensitization[7] acquires a new significance. It is reported in the London letter to the *Journal of the American Medical Association* that he has studied the significance and mechanism of the late inflammatory skin reactions to bacterial products which are seen in cases of bacterial hypersensitiveness. In the past, many workers have investigated sensitiveness to bacteria and their products but so far the mechanism of induced sensitization and the production of inflammatory skin reactions are by no means clear. It is thought probable that active antibacterial immunity and hypersensitiveness to bacterial products are brought about by two distinct portions of the bacterial cell. Harley has shown that the immunizing antigen of pneumonia can be obtained free from bacterial protein and other cellular substances and that it is this portion (the antigen) which is responsible for immunization. It appears that sensitiveness to bacteria is not induced by the immunizing antigen but by the bacterial protein and that the animal sensitized by either the whole organism or the bacterial protein reacts to these but not to the isolated immunizing antigen. Conversely, treatment of an animal with the isolated antigen produces immunity but not hypersensitiveness to the organism.

Johnston[8] resurrected the old autohematologic method to discover that sometimes the injection of whole blood into the muscle favorably influences the course of an eczema or of a psoriasis. The discomforts and the disadvantages of the injections, however, led him to abandon blood for urine. First rendering the urine as sterile as possible he administered it by subcutaneous or intramuscular injection. Believing that heat would destroy the allergens he sterilized the urine by the addition of antiseptics. His method was, first, to filter the urine thoroughly. Then an antiseptic was added and the urine allowed to stand for forty-eight hours. From such urines, cultures were made and only such urines as gave a sterile culture were used. Fifty cc. were made at one time and were kept under refrigeration until needed. Graduated doses were given every three or four days up to a maximum dose of 9 cc. Among the diseases treated were eczema, asthma, hay fever, urticaria, psoriasis, and pruritus. The best results were obtained in eczema.

If, then, we bear in mind what has just gone before, we not only see the problem in a more orderly light but we also realize more fully how far-reaching the problem is as we read the reports of its single phases.

E. Yen Gen and E. V. Skrotskiy[9] contend that the allergic state does something to children which predisposes them to scarlet fever. Using the Dick test as a criterion for predisposition and the intradermal injection of a 1 per cent watery solution of Witte's peptone as a test of the allergic state, they carried out observations on 516 children ranging in age from three to eight. They injected the peptone into one arm and simultaneously applied the Dick test to the other. The reactions of the two were quite similar (redness, swelling and pain) as was their time of appearance and disappearance. They ran a parallel course in 70 per cent of the cases. Fifty-three per cent of the healthy children reacted positively to the peptone but only 4 per cent of those convalescing from scarlet fever. Apparently scarlet fever desensitizes the organism to a nonspecific allergen. Fourteen per cent of the same convalescing children reacted to the Dick test. The authors conclude that the Dick test is of an allergic nature and that the state of allergy is a predisposing factor in the pathogenesis of scarlet fever.

Tate's article[10] on papular urticaria illustrates the loose thinking to which we have just referred. He assumes but does not prove that papular urticaria is a manifestation of allergy. He states that the disease is definite and distinct from urticaria and prurigo, that it occurs in the first four years of life, that it is aggravated by heat and by too much carbohydrate, that while digestive disturbances, teething and mild fevers are probably predisposing factors, nevertheless, they play but a minor rôle in the etiology. Rickets, he says, is not the cause. An underlying diathesis has not been demonstrated. Food does not excite the eruption. He believes that the exciting agent is some unknown factor connected with the home environment. He goes on. It is not the bedding or clothes, yet the agent can be carried by them. It is not due to vermin or to an antigen derived from human beings or animals. House dust is under suspicion, but has not yet been definitely proved at fault. Many times the eruption disappears spontaneously. Usually it disappears, or at least improves, when the child is removed from the home environment, as to a hospital, but often reappears when the child returns to the home.

Sulzberger and Vaughan[11] advance the theory that inhalants and the respiratory tract may play a definite part in the pathogenesis of atopic dermatitis and that contact alone with the irritating substance is not the whole story. Their experiments were conducted on a patient with atopic dermatitis which was made worse by wearing silk clothing. Cutaneous tests with an extract of silk allergen (1:50,000) were positive. The contact test, however, showed no reaction. The blood serum of the patient was injected intradermally into a nonatopic subject. Forty-eight hours later the injected subject sniffed a silk allergen powder into each nostril. In eighteen minutes the site of the serum injection itched severely and developed a large wheal. A contact patch test was negative.

There was an interesting letter and reply on "Urticaria and Trauma" published in the *Journal of the American Medical Association*[12] which gives a very good idea of the complexity of the question of allergy. The correspondent writes of a man of forty-two, a cornet player, who has been suffering for three years from redness, swelling and itching of any part of his body that is used or rubbed. If he has a head cold he develops a generalized, itchy, maculopapular rash. All the symptoms disappear spontaneously after one and a half to two days. There is no history of allergy. Patch tests are negative except for rye, peas, egg and lima beans. Omission of these from the diet has no effect. Are all of his symptoms allergic? the writer asks. The editor replies, that there are two possibilities present. One is that an underlying chemical allergy, such as food sensitiveness, is present and that the trauma is the precipitating factor in the production of the lesion. The other possibility is that it is a pure physical sensitiveness. "Even though the latter is the case there is still no reason why it should not be regarded as 'allergic', since allergy is essentially an abnormal response to a normal stimulus."

Dubbs' case[13] would seem to fall into the last category, i.e., although the manifestations

are those of a physical hypersensitiveness "there is no reason why it should not be regarded as allergic, since allergy is the abnormal response to a normal stimulus". Dubbs' case is that of a woman sixty-two whose skin when exposed to cold air or cold objects, developed itching and redness of the exposed parts. Perfectly typical wheals could be produced on any part of the body, at will, by the application of ice or other cold objects. If the patient walked briskly in the cold air, the skin symptoms would be accompanied by dyspnea and palpitation. The attacks never lasted more than five or ten minutes. The patient never had had any other form of allergy and her family history was entirely negative. The reporter notes that subcutaneous injection of epinephrin hydrochloride promptly relieved all symptoms and that fifteen grams of calcium lactate given three times a day caused a marked reduction in the intensity and frequency of the attacks. With the cessation of medication there was a return to the former status in quo.

Allergists have long considered asthma, eczema and urticaria as true examples of allergy and, from the study of them, have advanced various theories to explain the allergic phenomena. Now Vallery-Radot and Blamoutier[14] add to the long list of investigations. They use aqueous extracts of the spleen from which all possible albumins had been removed. They report that the injections were painless and, as a rule, provoked no untoward reactions. They further report that their best results were obtained in acute vesicular eczema. The results are said to have been rapid and sometimes lasting and permanent. In some cases the pruritus was modified although the eruption was unaffected. Dry eczema did not respond to the therapy. In urticaria of digestive origin they obtained results but cases of other origin were refractory. Quincke's edema was not influenced by the treatment. They report that frequently splenotherapy acted very favorably on the general well-being. They obtained cures in twenty-one cases of eczema out of forty-nine treated and improvement in twelve others. In thirty-five cases of urticaria treated they got cures in only eight and improvement in seven. Asthma was even less influenced than urticaria for they report that only four of seventeen cases were materially modified.

Most writers have busied themselves in explaining how a given disease is related to allergy. Browning[15] attacks the problem from an exactly opposite point of view in his paper on ringworm. Browning argues the thesis that ringworm of the extremities is a result or complication of hypersensitiveness rather than that hypersensitiveness is a complication of ringworm. He argues that the trichophyton finds lodgment because the "allergic balance", as he calls it, is disturbed. He asserts that when this allergic balance is destroyed measures directed directly against the trichophyton are unnecessary. Cure follows without them. He finds support for his theory of an "allergic unbalance" in the existence of other allergic manifestations or signs, especially in the skin. By treating the allergic state rather than the trichophyton he is able to report excellent results in thirty cases. He explains the good results obtained by ordinary treatment by the supposition that such methods restore the "allergic balance" to the affected parts. As further proof that his method of attack is logical and justifiable he points to the fact that his results were obtained in the face of the fact that the microscopic search for the fungus was positive in every case reported. Improvement, he says, usually begins within two weeks if the case has been correctly diagnosed and if instructions have been followed.

INDUSTRIAL SENSITIZATION

The compensation laws of the various states and countries have given a new importance to the various forms of cutaneous disease which arise from industrial and commercial products. Particularly have they given rise to an intensive search for the exact offending substance in these processes and compounds. For example, whereas not so very long ago we were content with the diagnosis of Baker's eczema now we must know just what substance it is which causes the dermatitis. It is no longer called eczema. Zitzke[16] reports that in 149 cases of Baker's dermatitis 41 per cent showed sensitivity to pure flour alone while 67.2 per cent showed sensitivity to chemically treated flour, as determined by the patch test. The chemicals used in treating flour are ammonium persulphate, calcium phosphate, and potassium bromate. Testing these three substances separately, it was found that the subjects reacted positively to the ammonium persulphate but were consistently negative to the calcium phosphate and potassium bromate. Hence Zitzke concludes that it is the ammonium persulphate which causes the dermatitis.

In view of the widespread use of hexylresorcinol by the laity there is interest in Dr. Walter's report of a case of sensitization to that remedy[17]. The patient was a woman who came of an allergic family, was allergic herself to strawberries and tomatoes, and who had two daughters who were subject to attacks of asthma. The patient had used hexylresorcinol dressings on a leg ulcer for five months. Later she used hexylresorcinol to clean out a wound on the hand. The result was a tremendous swelling of the hand with the formation of vesicles and large bullae.

Balsam of Peru has been used freely in our dermatological and surgical clinics without a thought of harm resulting. Yet Engelhardt[18]

reports that 2 per cent of people who have never had any skin disease or used ointments are hypersensitive to balsam of Peru and that 10 per cent of those who have had skin disease and who have used ointments are also sensitive. All of the constituents of the balsam are involved for they all give positive results to test reactions. Hence, Engelhardt concludes it is not advisable to continue the practice of using the balsam over large wound surfaces or in eczema. If it is desired to use it, he advises that patch tests be made first.

Tobias[19] writes that "perfume dermatitis" is not common in this country when one considers that thousands of bottles of various types and grades of perfume are sold annually. "Unfortunately the literature contains very few reports of true perfume dermatitis." These cases are fairly common in France, he says. Tobias describes three types of dermatitis which may be caused by perfume. The first type is dermatitis venenata which can be produced by the irritants in the perfume coming in contact with the skin at the first application without the intervention of hypersensitivity. He compares this type to the dermatitis produced by benzene or turpentine. The second type is that produced by specific ingredients of the perfume such as aldehydes, orris root, or dyes which, after long use, produce a specific hypersensitization (contact or eczematous dermatitis). A third type of perfume dermatitis was first described by Freund in 1916. This one is known as *Berlocque Dermatitis*. This form occurs as a streaked erythematous eruption which is followed by pigmentation. The cause is sunlight acting upon the skin through a film of the oil of bergamot, a common ingredient of toilet waters and cologne.

Tobias gives seven rules for making the diagnosis:

1. The location of the eruption. It occurs, naturally, on the regions to which the perfume has been applied. 2. Its sudden appearance. 3. Intense itching and burning. The intensity of these symptoms is usually out of all proportion to the extent of the eruption. 4. The time element. According to Sulzberger and Kerr there are two periods in the development of the hypersensitivity—(a) a period of incubation or formation of hypersensitivity which varies from months to years, and (b) the period of reaction which is usually constant, varying from twenty-four to seventy-two hours. 5. The type of eruption. The berlocque type is usually linear and followed by pigmentation after exposure to sunlight. The contact type is erythematous or vesicular. 6. The diagnosis by means of the patch test, as the sensitization is epidermal. 7. The history, elicited by close and repeated questioning.

Baer[20] in commenting upon Tobias' article relates that in connection with his study of lipstick dermatitis he had found methyl heptine carbonate to be the specific offending substance. He states that this substance is derived from ricinoleic acid and is widely used by perfumers for its violet odor. Baer found that over 50 per cent of both men and women were sensitive to it. The patch test was the proof.

CANCER

For years the debate has been going on as to when a carcinoma is not a carcinoma. Is cancer always a cancer and if not, when does a one time benign growth become cancerous? Sutton[21] debates these questions in a very interesting fashion. He is inclined to believe that, at least in many instances, cancer is cancer from the start. He begins his article by quoting a case to substantiate his thesis that "cancerous lesions come into existence on sites previously normal, a common experience". He agrees with Broda that "the entity called carcinoma, regardless of etiology, is a primary disease of epithelial cells and all other phases and sequelae, though of great importance, are in reality of secondary nature".

Sutton has done an enormous amount of research on the subject but acknowledges that all such work is of necessity incomplete. In order to make such work complete one should have started with the normal skin and have followed its various changes through to actual, demonstrable cancer formation. Naturally, one cannot do this. Instead one must be content to study specimens taken from various persons and from various growths. As one cannot follow through the evolution of the cell in one patient, one must be satisfied with a series of static pictures taken, so nearly as one can manage, from growths of various ages. In spite of this insurmountable obstacle, Sutton has studied enough cases to have reached certain very definite conclusions.

"1. (a) Many cancers begin as de novo lesions. (b) The earliest visible lesion in these cases is a circumscribed, scaly, epithelial new growth.

"2. (a) The structure of many minute, scaly, epithelial new growths is such that it is reasonable to presume that, if not interrupted, they would become obvious carcinomas. (b) It is reasonable to believe that such lesions are in fact early carcinomas. (c) If a lesion has a structure not compatible with a likelihood of its being early carcinoma, it might be called precancerous. But it would be impossible to predict that such a lesion might, if not interrupted, develop a structure such that it would be properly called carcinoma.

"3. (a) It is impossible to determine at what point in its natural history a cancerous lesion is not cancerous. (b) It is reasonable to

believe that cancer is cancer from the start.

"4. The concept of precancerosis is indecisive and undefinable. It groups unrelated conditions which may or may not be early cancer. Its acceptance entails an insoluble problem of a dividing line between cancer and not-cancer, as well as a statistical assay of lesions that are strictly individual.

"5. (a) A lesion may be cancerous independently of its size and rate of growth. (b) Cancer is primarily an epithelial disease. (c) Cancer consists of mutated somatic cells. (d) The earliest visible manifestations are circumscribed, dyskeratotic lesions which microscopically are composed of polymorphous epithelial cells that proliferate, keratinize and undergo mitosis in an abnormal manner. (e) Malignancy depends on a balance between proliferative capacity of its cells and the control or resistance of its host. (f) One tumor may contain several kinds of cells as a result of mutation following on mutation."

Riecke[22] describes a rare form of cutaneous carcinoma in a woman of sixty-two. The first manifestation occurred a year before when a nodule appeared on her thigh. The nodule enlarged and suppurated. An erysipelatous process developed, after which fresh nodules appeared accompanied by a severe swelling in the groin which perforated. Fresh nodules continued to appear which always followed the same course, softening, disintegration and an exudate of serous fluid. Various diseases were considered in the differential diagnosis such as syphilis, tuberculosis and blastomycosis. After observation and study these diagnoses were rejected and Riecke became convinced that the disease was an abnormal form of cutaneous carcinoma. This conclusion was confirmed by the microscopic examination which disclosed a basocellular carcinoma. Riecke has seen one similar case.

Franseen and Taylor[23] report nine cases of carcinoma unquestionably due to arsenic, five probable cases and one case in which only keratoses developed. They state that arsenic may be deposited in the skin and there manifest its carcinogenic powers as late as forty years after the exposure. In their opinion the carcinogenic property of arsenic is not properly appreciated so that cancer is sometimes produced by accident. Fowler's solution, the inorganic trivalent form of arsenic, seems to be the chief offender. Chronic arsenical lesions seem to be rare after the administration of the organic compounds. While the squamous cell carcinoma is the ordinary type, more than one third of all arsenical carcinomas are said to be of the basal cell type. Although the malignancy of the squamous carcinoma is low, metastases are not infrequent. Hence the writers advise that the regional lymph nodes should be removed in all cases of growths of considerable size.

Laboratory workers have now for a long time used mice in the study of cancer and by such studies have added much to our knowledge of human cancer. Mottram's article[24] on the relationship and the rapidity of the growth of tar warts in mice has, therefore, much of interest to us. Analyzing the time of appearance in its relationship to malignancy, Mottram found that malignant warts appear more slowly after the tarring than do the benign. So too, he found that warts which appeared late grew faster than those which appeared early. Sessile warts are largely malign whereas pedunculated and horny warts are usually benign. Sometimes a sudden increase in growth was noted and in all such cases the wart was found to be malignant. As a rule, he states, benign warts grow slowly and malignant warts grow rapidly. Moreover he found a close relationship between ulceration and malignancy. Mottram's statement that "autografts show that there is a continuous development and change in warts from benign to semimalignant, from semimalignant to malignant" bears out Sutton's[21] contention that cancer may arise de novo and that cancer is cancer from the start.

Dunn and Smith[25] report the unusual case of a primary squamous carcinoma which healed itself. They had had a somewhat similar case once before in which, however, the spontaneous healing was surmised but not seen as the growths were surgically excised. In the reported case a young man presented multiple lesions which had been in existence for seven years. In all that time there had been no metastasis. Sections of tumors in the early stages showed a highly malignant looking condition. Sections taken later in the disease showed an increased differentiation of cells and more complete cornification of the pearls. Finally there was healing with scarring. The writers believe that such cases as these may not truly be cancer, yet, in their early stages, they cannot be differentiated from it, either histologically or clinically.

In the field of roentgentherapy, investigation still continues as to when it can be used to the best advantage and as to method. More and more articles are written to prove that in certain types of carcinoma the reason for the failure to cure is inadequate irradiation. Hintze[26] is one of the more recent writers on the subject. He reports his observations on seventy-one cases of what he calls persistent carcinoma, that is to say, cases which five years after treatment by surgery or irradiation have not become free from symptoms or, having been free for a time, have relapsed. Thirty-nine of his cases had been treated first by surgery and thirty-two by irradiation. Sixty-two of the seventy-one cases were on the face. Four cases had been

treated exclusively by surgery. Hintze calls attention to the fact that not one had been cured by this method. On the other hand, of thirty-five patients who had first been treated by surgery and then by irradiation nineteen were cured. Of seventeen patients who were treated by irradiation in other clinics one case was cured by surgery and four by irradiation in his own clinic. Of fifteen patients who were treated first by irradiation, in his own clinic, nine were not cured because there were multiple lesions. In six of the fifteen the primary focus persisted or relapsed. Under later treatment in his clinic eight of the nine multiple cases were subsequently cured. Two of the relapsing cases had been treated by the old method of small doses and one by medium doses. Not one had received a large dose at the very first treatment. These figures cause Hintze to say that the reason that carcinoma persists after irradiation is that the primary dose has not been large enough.

Hintze's conclusions would seem to be at variance with those of Dr. Frank[27]. Reporting to the Vienna Society for Roentgenology, Frank gave the details of his investigation. The carcinomas were large and of the pavement epithelium type. "Half of the tumor was irradiated with one large dose (1,800 roentgens) while the other half was irradiated daily with a so-called fractional dose of 200 roentgens until a total of 4000 roentgens had been reached. The quality of the rays and the roentgen minute dose were the same. By the time 1000 roentgens had been administered to the side that had been given the fractional irradiations, a considerable decrease in the size of the tumor was noticeable, while the side to which the single large dose had been given showed no macroscopic signs of a change in spite of the fact that the surrounding skin, which had been exposed to this irradiation, reacted noticeably. When 1800 roentgens had been reached, the same dose that the other side had had, the tumor had largely disappeared on the side irradiated with the small doses, while on the other side macroscopic changes were still lacking. In the further course it was observed that on the side to which the single large dose had been applied the tumor was still partly in evidence while it had completely disappeared on the side to which the fractional doses had been applied. Histologic studies revealed that on the side of the fractional irradiations the tumor cells were destroyed by undergoing cornification and maturation while on the side of the large dose a vacuolizing degeneration took place. Studies conducted in several other suitable cases led to the same results. In view of these observations Dr. Frank formulated the thesis that the application of a single large dose leads to a less rapid disappearance of a tumor than the fractional irradiations. This factor is important when the danger of metastasis is considered, for it has been assumed erroneously that in cases of fractional irradiation the danger of metastasis is greater." Among the listeners to his report many agreed that fractional irradiations are generally to be preferred.

TUBERCULOSIS

The controversy as to whether erythema nodosum is of tuberculous origin goes on with unabated energy. The debate is still indecisive with, however, the weight of evidence favoring the negative side. No one has yet reported a respectable number of cases, a number large enough from which to draw many conclusions; nor has any one as yet put together all reported cases to make up an impressive total. In our search we find many papers based on one case and but one on as many as thirty.

As examples of the papers of the proponents we have chosen those of Moritz and Lederer, Deaner and Aguirre.

Moritz and Lederer[28] imply rather than say that they believe the erythema nodosum is due to the tubercle bacilli. They base their opinion on a comparison of the capillary changes in erythema nodosum and in positive tuberculin test tissue. They found that in fifteen cases the changes were identical in the disease and in the test.

Deaner[29] must also be classed with the proponents although he reports but one case. A woman, aged twenty-nine, had been in contact with a tuberculous sister for six months. An x-ray of this woman showed the picture of an acute disseminated tuberculosis. Occasionally she had a slight rise in temperature. The only other sign she had which pointed to tuberculosis was a well-developed erythema nodosum.

Aguirre[30], reporting a series of only eight cases, draws the very definite conclusion that "the results of his work, by which the presence of tubercle bacilli in the erythematous nodules was verified, constitute the most complete bacteriological proof of the tuberculous origin of erythema nodosum." He reports that, in five cases out of eight, material from the erythematous nodule yielded the tubercle bacillus on culture. The material in one of the three negative cases was taken from the nodule by biopsy fifteen days after the appearance of the nodule. The material in the second negative case was taken from a guinea pig which had been inoculated six months previously. The investigation was halted in the third negative case because of infection among the animals.

Opposed to these writers are the opinions of Lemming, of Nobecourt and Ducas and of Goldberg-Curth.

Lemming[31] reports thirty cases of erythema nodosum all of which occurred in patients with a past history of tuberculosis and nineteen cases

of recurrent erythema nodosum. As a result of his studies he concludes that the disease is an allergic expression of an active tuberculous infection. According to him, the presence of active tuberculous disease should be ruled out by careful examination. Erythema nodosum, he elaborates, may be the exogenous reinfection with the tubercle bacillus. It may be a superinfection or it may be present as a result of a grave active pulmonary tuberculosis in which the deficient antibody formation results in a state of anergy.

Nobecourt and Ducas[32] believe that the erythema nodosum lesions in a case of theirs were the result of a hyperallergic state in spite of the actual evidences of tuberculous foci in the patient. The father of the patient had died of tuberculosis. On the patient herself the tuberculin test was positive and injections of her blood into a guinea pig gave rise to tuberculosis of the inguinal glands.

Goldberg-Curth[33] does not dispute that erythema nodosum is often seen in association with positive tuberculin reaction tests and even with clinical and roentgenologic signs of pulmonary tuberculosis. Extrathoracic tuberculosis is a rather rare accompaniment of erythema nodosum, she writes. She prefers to say of erythema nodosum that it is a cutaneous reaction to an infection whose pathogenic organism is unknown. She says further, that symptomatic erythema nodosum may develop in the course of nearly every infectious disease and as a cutaneous reaction to toxic substances. She admits that, in childhood, the majority of cases, not all, are closely related to a tuberculous process. As to the demonstration of tubercle bacilli in the blood or in cultures made of material taken from the nodules, she does not admit that these are definite proof of the tuberculous nature of erythema nodosum. (Compare Aguirre above.) She does think that all forms are an indication of an allergic change in the organism. In short, she rejects the hypothesis that erythema nodosum is a true form of tuberculosis but agrees that cases do occur, although rarely, which present the clinical aspect of erythema nodosum and the histopathologic aspect of tuberculid.

The same reasoning which we have just seen applied to prove that erythema nodosum is or is not a tuberculous process we also see applied to prove that other diseases which occur more or less frequently in association with admitted tuberculosis are themselves tuberculous. For instance, Dr. D. W. Montgomery publishes[34] a case of lichen scrofulosorum which occurred coincidentally with lupus erythematosus. The latter occurred in close proximity to typical lesions of the former. This, he believes, indicates more than mere coincidence. Therefore, as lichen scrofulosus is admitted to be tuberculous the deduction is justified in this case, he declares, that the lupus erythematosus is also tuberculous.

MacKee and Sulzberger[35] have published an interesting article on one of the rarer forms of tuberculosis, the rosacea-like tuberculid of Lewandowsky. This form has been known in Europe for some time but has apparently escaped recognition in this country. It differs from rosacea in that it has a tuberculoid structure and is essentially papular, but it resembles rosacea in that it shows erythema and telangiectasia although in lesser degree. The writers report that the subjects of the disease are very sensitive to quantitative intradermal injections of tuberculin. The disease responds well to injections of gold and sodium thiosulphate, to a high vitamin diet, general tonics, generalized irradiations of ultraviolet light and to intradermal injections of tuberculin. Hence it is important that this disease should be distinguished from rosacea which it resembles.

Wile and Grauer[36] report five cases of the same disease all of which were in women. Histologically, the changes were, in every instance, tuberculous. Some cases presented a state of anergy. Wile and Grauer believe that the disease is a true tuberculosis of the skin and is the end result of a hematogenous spread from an underlying focus.

TREATMENT

The number of reports having to do with the treatment of disease have been so numerous during the past year as to give the impression that more attention is being paid to this important field. Then too, the wide range and great variety of diseases considered are striking.

In our last report of Progress (*New Eng. J. Med.* 211:1200 [Dec. 27] 1934) we noted that trichophytin was advocated for the treatment of dermatophytosis. Now we note that Traub and Tolmach[37] are not so enthusiastic about it as the earlier reporters. They studied the effect of trichophytin in 135 cases of dermatophytosis, the majority of which at the time of treatment were accompanied by dermophytids. Fungus infection of the skin accompanied by the latter should, according to immunologic concepts, offer the most ideal means for evaluating trichophytin. The authors obtained fourteen cases of apparent cure. Some of these presented an early recurrence; in some the cure was questionable. There were varying degrees of improvement in fifty-eight cases. In sixty-three there was no change at all apparent. In those cases in which no improvement was obtained with the treatment, the application of salves such as Whitfield's ointment, etc., was followed by results. The authors conclude that trichophytin exerts little if any effect on the course of trichophytosis.

So, too, we find that dermatologists are awake

to the newer results in other fields of medicine. Pusey and Rattner[38] describe a dermatosis which closely resembled discoid lupus erythematosus in which they used organotherapy. It occurred in a woman and became especially pronounced with the menses. Based on evidence indicating that the adrenal cortex has a decided influence on the gonads, 2 grains of desiccated whole substance (adrenal) was given t.i.d. Improvement of the lesions followed and the exacerbations during the menses were no longer apparent.

Sézary and Horowitz[39] report their investigation of the therapeutic effect of an ovarian extract mixed with the patients' own blood. The extract is added to 20 cc. of blood and is injected intramuscularly three times a week until a total of twelve injections has been given. That they called a course. Sometimes they administered as many as three courses. Their best results were obtained in scleroderma which had appeared in patients who were approaching the menopause. One case entirely recovered. Five cases gave varying results.

The present-day attitude relative to the value of gold and of bismuth in lupus erythematosus therapy is well represented by Smith[40]. For purposes of comparison, he divided his twenty-four patients into two equal groups. One group received the gold therapy and the second group the bismuth. Then he compared the results. Gold cured more than bismuth, but bismuth improved more cases than gold. Bearing these results in mind he selects bismuth as his choice because it is less toxic, less expensive and less inclined to light up or aggravate an existing tuberculosis.

Gouin and Bienvenue[41] reported the result of their rather new technic in using gold salt therapy in cutaneous tuberculosis which they employed in nine cases of disseminated lupus, two of lupus verrucosus, six of tuberculous ulcers and three of tuberculous adenitis. First, the lesions were opened by curettage, so that they could be subjected to the action of light and air. Each time that an injection of gold was given the lesion was scraped under anesthesia, unless meantime the lesion had cicatrized. Under this method they found that five or six injections of 0.15 Gm. gold sufficed to effect a cure.

MacKee and Cipollaro[42] have made an important addition to the precautions to be taken in roentgentherapy by calling attention to the general lack of a uniform, standard unit of measurement among roentgenologists. They advise the use of a Victoreen dosimeter and of reference to its unit as a "roentgen". Whereas today it is common to refer to the various factors in an epilating dose, for example, as 2 min., 3 ma. 100 kilowatts, distance 8″ if the "roentgen" unit method were used, the simple statement that the dose was one of 300 roentgens would include all these factors. They give as another sample a patient who is said to have received one quarter of a unit. MacKee and Cipollaro would have the dose described as one of 75 roentgens. The adoption of such a unit as the "roentgen" would make for accuracy of description and also for clarity.

One of the most obstinate and at the same time alarming mishaps which the roentgenologist has to treat is a Roentgen ray dermatitis. Craps and Alechinsky[43] report a method of treatment, which they say, is simple to use and which gives quick results. They tried their method on five patients in all of whom the response was good. First, they cleanse the affected area with ether and also remove all squamae and crusts. Then they paint on a 5 per cent aqueous solution of silver nitrate. Now the whole is irradiated with a quartz lamp at a distance not greater than 20 cm. for from five to ten minutes. This should be sufficient to dry the affected area completely and to make the nitrate turn a deep black. If it is not a glistening black, the painting and drying must be repeated. A dry sterilized gauze dressing is all that is needed to cover the area. Ointments must not be used.

Carty[44] is convinced of the superiority of the elastic adhesive plaster over all other methods in the treatment of bed sores. He declares that, by this method, he can heal a bed sore in fifteen days. He takes two pieces of elastic adhesive pieces an inch wider than the sore. These he puts on the ulcer, overlapping its edges, one above the other. The dressing is left in place until it comes away of itself when, after wiping away any discharge present on the surface of the ulcer, it is replaced.

The treatment of warts still intrigues the medical mind. Shellow[45] has treated ninety-seven lesions in seventy-three patients with local injections of a 15 per cent solution of bismuth sodium tartrate. The wart is first cleansed with soap and water and then with iodine and alcohol. With a fine hypodermic needle, from ½ to 2 minims of the bismuth tartrate solution is injected from the side into the base of the wart. In from one to three days a dark hemorrhagic spot is visible through the keratotic area. At the same time the pain in the lesion, if there was any, disappears as does the peripheral redness. In fourteen to seventeen days after the injection the wart has flattened, the hard keratotic tissue has been thrown off and a smooth, healthy surface has resulted.

Cornbleet[46] has reported very favorably on the effects of maize oil administered by mouth to patients with eczema. By eczema they mean a condition which started in infancy and has persisted ever since with exacerbations and remissions. This condition, they say, is usually referred to as allergic, exudative and diathetic

eczema, Darier's prurigo or generalized neurodermatitis. They consider the results unusually good. A few patients had asthma as well as eczema and the asthma was benefited as well as the eczema. The results seem permanent, for there have been but few relapses during the four and a half years they have been using the oil. Some patients who have had eczema since infancy have remained well for three years or more. The oil is administered by mouth and preferably chilled a little to make it more palatable. At first the dose is one tablespoonful taken before or after meals. Gradually the dose is increased until the patient is taking four tablespoonfuls three times a day.

Nichols writes[47] that by his method more than 80 per cent of the cases of acne in adolescent children can be controlled if their cases are seen early. The method consists chiefly of keeping the skin rather chapped by the use of soaps, at first mild but later stronger, and of whitewash of increasing strength. At bedtime the face is washed with mild castile soap and fairly hot water. Then the skin is sopped for five minutes with lotio alba, one-fourth strength, which is allowed to dry on and remain overnight. As the skin becomes accustomed to the treatment, the strength of the soap and the wash is gradually increased. If the skin becomes overdry the treatment is suspended for a few days to allow it to soften. Graduated sun exposures and ultraviolet light irradiations are very helpful adjuvants to the treatment. Nichols reports that, in thirty-seven children out of forty-seven the acne is virtually invisible or is well under control after treatment of from three months to four years.

The results with germanin (Bayer 205) in the treatment of pemphigus do not seem very encouraging. Its employment in pemphigus is said to rest upon the remedy's successful use in trypanosomiasis and upon the alleged resemblance of trypanosomiasis to pemphigus in that both are chronic, both have remissions and both have fever. It is stated by Tobias[48] in an article on "Juvenile Pemphigus" that many cases which at first showed a remission or an improvement later developed a recurrence and died. Other cases developed an exanthem and nephritis. The drug is given intravenously in a beginning dose of 0.3 Gm. which is gradually increased to as high as 1 Gm. After five doses a course has been completed. Tobias reports the case of a girl, five years old, who received the drug. She presented a definite improvement with the first course. A recurrence necessitated a second course. The child developed a septicemia and died.

Craps and Alechinsky[49] report a rather unusual treatment of such cutaneous lesions as a trophic ulcer, an infected traumatic ulcer, varicose ulcers, ulcerated syphilitic gumma and an ulcer resulting from the curettage of a large tuberculous verrucous lesion of the palm. For the treatment of these various types of ulceration they used direct applications of an aqueous solution of histidine, 1:1000, made daily. In general, the ulcers became clean very rapidly and soon took on a good color. The skin tolerated the histidine well.

Beerman and his associates[50] call the attention of dermatologists to Dioxyanthranol 1-8 as a substitute for chrysarobin. The drug was introduced into dermatology in 1916 under the trade name of "Cignolin".

The Council on Pharmacy and Chemistry of the American Medical Association says of it[51] that it is made by the reduction of dioxyanthraquinone, an easily available substance used in industry and gives as its formula, $C_{14}H_{10}O_3$. The formula for chrysophanic acid, which it is proposed to displace with dihydroxy-anthranol, is given as $C_{17}H_{10}O_4$. The manufacturers have suggested "Anthralin" as a name for the drug and this name has been accepted by the Council.

Anthralin is described as "a yellowish, crystalline powder, practically insoluble in water but readily soluble in the more complex and lipoid solvents—a feature of distinct advantage in the preparation of ointments, lotions and pastes. Its color is probably least noticeable in petrolatum album which provides for it an economical and satisfactory ointment base". Anthralin has been used only for external applications in concentration of from 0.1 per cent to 5 per cent. A very weak concentration is always used first to test out the patient's tolerance. That discovered, the strength of the application is gradually increased.

Beerman, Kulchar, Pillsbury and Stokes[50] have used Anthralin in a great variety of diseases but with especial satisfaction in psoriasis and in mycotic affections. They state that the safe effective range of concentration is from 0.1 per cent to 1.5 per cent. Most of their results were obtained with 0.5 per cent although it was occasionally necessary to raise the strength to 1 per cent. A 2 per cent preparation has been known to produce a severe dermatitis occasionally. "The advantages claimed for dioxyanthranol 1-8 include the following: 1. Definite chemical composition and economical synthesis from an available material. 2. Effectiveness in very low concentrations (from 0.1 to 2 per cent). 3. No constitutional symptoms such as renal irritation in these low concentrations. 4. Limitation of dermatitis—inducing action to the area of application without tendency to extension or generalization. 5. No production of conjunctivitis even when used on the face or scalp. 6. Comparatively little discoloration of clothes or skin and practically no discoloration of hair in the concentrations employed."

Beerman's report of the use of Anthralin on the scalp is very striking. Of twenty-nine cases eighteen underwent complete involution, fifteen within five weeks.

On the body it was rarely necessary to use a concentration stronger than 0.5 per cent and treatment was usually begun with a 0.1 per cent. Complete involution was obtained in twenty-three cases within four months, sixteen of them within five weeks. Other cases were improved from 40 to 90 per cent in a comparatively short time, in three months or less. Only one case was entirely resistant.

The list of other diseases in which Anthralin has been successfully used is long and imposing. Especial attention should be given to its success in combating mycotic diseases. Indeed, a number of Europeans are quoted as believing that it is in this field that Anthralin finds its greatest usefulness. Beerman and his coworkers, however, rate its usefulness in psoriasis first and in mycoses second.

In conclusion, they say that "Dioxyanthranol is not proposed as a new drug nor one completely free from the objections familiar in the use of chrysarobin. It is none the less, we believe, a superior substitute which deserves greater popularity now that it can be made readily available in this country."

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CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 22021

PRESENTATION OF CASE

A forty-two year old white American was first seen complaining of chest discomfort.

The patient had always led a fairly sedentary life until about ten months previously. At that time he began to indulge in boxing and tennis as a means of exercise. Shortly thereafter, while playing tennis, he noticed that he would feel discomfort across his chest, equally distributed on both sides and not radiating. This was associated with a sensation of fatigue in both arms to the elbows. There was no breathlessness or palpitation. The discomfort subsided spontaneously after a minute or two and he never discontinued activity because of it. During the succeeding four or five months he suffered from similar attacks twice daily, particularly when walking uphill. These subsided promptly after resting for a few seconds. He consulted a physician who found no abnormality. An electrocardiogram was negative. Thereafter he continued to have recurrent attacks with moderate exertion but noticed that he was more prone to have them shortly after heavy meals and smoking. He lessened the amount of tobacco used from six to ten pipefuls daily to one and a half. This appeared to diminish the frequency of the attacks, and activity which had previously caused distress no longer did so.

His father died suddenly of heart disease at the age of fifty. His mother was living and had pernicious anemia.

At the age of ten he had had scarlet fever which was believed to have affected his heart.

Physical examination showed a well-developed and obese man who did not appear ill. There was very slight arcus senilis. The hair was partly gray. The pupils were equal and reacted normally to light and distance. The left border of cardiac dullness extended to, and the apex impulse was felt eight centimeters from the midsternal line in the fifth interspace. The right border was at the sternal margin. The sounds were regular and there were no murmurs. The pulse was 72. The peripheral arterial walls were soft. The blood pressure was 130/85. The lungs were clear. The edge of the liver was felt at the costal margin. Knee jerks were absent.

An electrocardiogram was normal.

X-ray examination of the chest showed normal heart contours. The aorta was normal in width but the knob was considered slightly prominent for his age.

The patient was advised to limit his activities and to continue his limitation of tobacco, using the occurrence of symptoms as a criterion. One month later he reported that he was completely relieved of chest discomfort. Thereafter he suffered distress occasionally but only with overexertion.

About one and a half years later while indulging in moderate but not unusual exercise he suddenly fell unconscious and died shortly afterward.

DIFFERENTIAL DIAGNOSIS

DR. HOWARD B. SPRAGUE: With no more than the ordinary mental reservations that one makes in cases of this sort I should say that Dr. Mallory was playing ball with me this time.

To summarize, we have a relatively young man who has always led a sedentary life but suddenly decides he must have exercise and goes in for boxing and tennis. Shortly thereafter he finds that tennis brings on a sensation of discomfort in the chest and fatigue in the arms and he finds beyond that that exercise such as walking uphill also brings on the sensation. So far as I know, that sensation is angina pectoris. He consults a physician who examines him and finds a negative electrocardiogram and a physical examination which is not very significant. He has a rather bad family history in that his father died suddenly at the age of fifty but other evidence pointing to cardiac disease is very slight. There is a note that he has very slight arcus senilis. We always mention the occurrence of that sign but you can get any sort of figures that you want indicating that arcus senilis has something to do or nothing to do with arteriosclerosis. It has been thought by some to be associated with a certain type of individual with hypercholesterinemia and to be associated with arterial changes. I, myself, must confess that I am impressed when finding arcus senilis, perhaps particularly at this age. There is a little prominence of the aortic knob. He is said to be obese but the physician was able to find the apex impulse of the heart which means that the patient was probably not very obese or that the examiner was particularly dextrous.

The patient himself noticed that reduction of activity and reduction of tobacco had some effect in increasing his ability to exercise without discomfort and in this clinic I think our feeling is that tobacco in cases of angina pectoris should be reduced or omitted if possible. That feeling is not held so strongly by some other clinics.

The patient gets along very well and a year and a half later, indulging in moderate exer-

cise, becomes suddenly unconscious and dies shortly after, meaning that there may be slight delay between collapse and death. Suddenness after all is a relative thing.

DR. TRACY B. MALLORY: The interval was less than five minutes.

DR. SPRAGUE: He has no evidence of valvular disease or lues. The knee jerks were absent but with the presence of active pupils I think that is not of any particular importance unless we go into the details of whether reinforcement was tried, and so forth.

I am not going to do anything but mention the routine possibility of dissecting aneurysm which comes up at every case. I do not believe he had that. He died of angina pectoris. He died so suddenly that there would not be cardiac infarct, but just what we shall find in the coronary circulation, I do not know. He undoubtedly had advanced coronary disease but whether diffuse or localized in one of the main arteries or ramifications, I cannot tell. I do not know that we can say actual occlusion of a coronary artery will be found because apparently recent unpublished evidence of Dr. Robert Levy of New York seems to show that the finding of actual occlusion of the coronary artery in death of this sort is the exception rather than the rule. The patient died from a coronary spasm or the result of coronary insufficiency leading to a standstill of the heart or possibly to ventricular fibrillation; so that I think the diagnosis is arteriosclerotic coronary disease, with death from angina pectoris, and possibly with coronary occlusion as the terminal event.

CLINICAL DISCUSSION

A PHYSICIAN: Will you say a word about the normal electrocardiogram?

DR. SPRAGUE: Unhappily, about twenty per cent of patients who come to our clinic with the symptom of angina pectoris have entirely negative findings,—electrocardiogram, physical examination, x-ray and the rest.

DR. PAUL D. WHITE: One of the points of special interest in this case was the relationship of his symptom to tobacco. He, himself, thought that he had "tobacco angina" and hoped that that would be our diagnosis and that he might be passed for life insurance. Probably one should not make such a diagnosis as "tobacco angina". Although tobacco undoubtedly has an important influence in some individuals and aggravates their angina pectoris, it cannot alone be blamed for the angina pectoris in this man. The final result proved that.

The first instance of electrocardiographic proof of a specific effect of tobacco on the coronary circulation that I have had any knowledge of was handed to me by Dr. Starr of Hartford, Connecticut, a year or two ago. He is here and I wonder if he will say a word about that case.

DR. ROBERT STARR: That case was a boy about eighteen years old who had used tobacco for perhaps two years previous to the time I saw him. Two or three months before I saw him he was in training for basketball, injured himself, gave up training and went back to smoking and noticed that cigarettes after the intermission always made him dizzy. He was sent to me by Dr. Kingsbury, who examined him because of this dizziness and found the physical examination to be essentially negative. The blood pressure was normal, everything was normal. I took an electrocardiogram before he smoked, then had him smoke a cigarette and repeated the electrocardiogram, and when the records were developed they showed a very definite negative T wave after smoking. I asked him to come back and on the second visit I started the electrocardiograph going just before he began to smoke; every ten seconds or so I would take a tracing and it was evident that the T wave became negative at the time of his dizziness and returned to normal afterwards.

DR. MALLORY: I think that is a very interesting observation. So far as the peripheral arteries are concerned, the effect of tobacco is very obvious. Cases of Buerger's disease and Raynaud's disease usually show very marked increase in spasm during and for a considerable period following smoking.

DR. WHITE: Stimulated by this observation of Dr. Starr's we have begun a study, which is now in progress, on the effect of the inhalation of tobacco smoke on the electrocardiograms of normal individuals and of those with coronary disease or angina pectoris; there have been some definite changes but not so striking as in Dr. Starr's original case. The rapid inversion of the T waves in lead two in that case makes us believe that certain individuals doubtless have a special coronary sensitivity to tobacco with spasm; it may prove worth while to test individual cases in the laboratory by electrocardiography to see if there should be a reduction or complete omission of tobacco in their treatment. We shall make a full report of this study at a later date.

CLINICAL DIAGNOSIS

Coronary heart disease.

DR. HOWARD B. SPRAGUE'S DIAGNOSES

Arteriosclerotic coronary disease.
Angina pectoris as the cause of death.
Terminal coronary thrombosis unlikely.

ANATOMIC DIAGNOSES

Coronary sclerosis, marked.
Acute atheromatosis: Aorta, mitral valve.
Myocarditis, fibrous.

PATHOLOGIC DISCUSSION

DR. MALLORY: The postmortem examination on this case showed what Dr. Sprague predict-

ed. There was a very severe grade of coronary sclerosis present throughout all branches of the coronary arteries but most marked in the descending branch of the left, which was reduced to barely one-tenth of the normal diameter. There was no thrombosis. The blood was fluid throughout all the vessels, and I would second the point that Dr. Sprague made that relatively sudden deaths rarely show coronary thrombosis. They always show diseased coronaries but there is no complete obstruction. In other words it definitely is an anginal death and not a death from coronary thrombosis.

He showed rather more than the average amount of arteriosclerosis in the aorta and some of the other organs. The heart was not hypertrophied. On section we could make out grossly minute areas of scarring, one or two millimeters in diameter, scattered throughout the myocardium but definitely most numerous in the region supplied by the descending branch of the left coronary. Microscopically this was confirmed by finding small areas of fibrosis where the muscle cells had entirely disappeared. These were evidently quite old, however, and there was no sign of any fresh, recent degeneration of the heart muscle. The case was checked with examination of the head, where nothing that would explain any acute death was found.

CASE 22022

Presentation of Case

First Admission. A forty-nine year old Polish landscape gardener entered complaining of difficulty in breathing and "turning black" for two weeks.

Twenty years before entry the patient began having asthma every winter beginning about the fifteenth of November and lasting off and on until the following May. The attacks never occurred at night but seemed to be precipitated by cold air. They usually were associated with cough and the production of small amounts of blood-tinged sputum. There was no past history of any other allergic manifestations. Two and a half years before admission he had a chest cold associated with a marked coryza. He coughed considerably with the production of a slightly blood streaked thick mucoid sputum. He remained at home and recovered in about two to three weeks. Since then he became increasingly dyspneic, especially upon climbing stairs. He also developed slight blurring of vision, occasional headaches, tinnitus, and vertigo. One year before admission he noticed that his face, lips, cheeks, and fingers were bluish. Five months before admission he again developed a chest cold, entered a hospital, and was told there that he had a blood disease. A pint of blood was withdrawn following which he felt worse and was put into an oxygen tent. He left the hospital after three weeks and returned to work. His shortness of breath continued but was not so severe. Two weeks before admission, after a slight cold, it became almost impossible for him to breathe, expiration being especially difficult. He had marked dyspnea even on walking very short distances and felt exhausted all the time. There seemed to be a constant pressure in his chest, as if he were being squeezed. He noticed that his hands, especially his fingers, and his face and lips were becoming very blue and at times suggested a real black color. He experienced cramps in the calves of his legs upon the slightest movement. His ankles became slightly swollen. He wheezed considerably and a fairly marked degree of orthopnea developed. During the past five months he lost about fifteen pounds in weight. Recently he had been taking two glasses of whiskey every night which he believed had helped his condition.

His mother had asthma.

The past history is negative, except that five years before entry he had worked one summer with broken rocks in building a road.

Physical examination showed a well-developed and nourished man lying in bed in no apparent distress. His breathing was abdominal in type. There was marked cyanosis of the lips, face, hands, and feet. The mucous membranes were highly colored; the fundic veins were very dark. There was marked pyorrhea. The tonsils were slightly enlarged and highly colored. There was slight dorsal kyphosis. The chest was barrel shaped and the motions were scarcely perceptible during respiration. The lower chest wall was drawn in with inspiration. Scattered over both lung fields were numerous crackling râles. The breath sounds and tactile fremitus were diminished. The heart was not enlarged to percussion although the right border was 4 centimeters from the midsternal line. No murmurs were heard. The blood pressure was 134/80.

The temperature was 99.2°, the pulse 88. The respirations were 15.

Examination of the urine was negative. Examination of the blood showed a red cell count of 7,990,000, with a hemoglobin of 120. The white cell count was 11,000, 81 per cent polymorphonuclears. The stools were negative. The vital capacity was 600 cubic centimeters and after adrenalin 1200 cubic centimeters. Other determinations showed a vital capacity of 1,000 to 1,200 cubic centimeters before adrenalin and 1,300 to 1,700 cubic centimeters after adrenalin.

X-ray examination of the chest showed an enlarged heart both to the right and left of the spine and prominent lung markings.

He improved subjectively somewhat on ephedrin and potassium iodide and was discharged twelve days after admission.

Second Admission, six months later.

During the interval he did fairly well, continuing with ephedrin and potassium iodide,

and had not been completely incapacitated. Six weeks before admission his asthma became worse and he was forced to take adrenalin almost every day for relief. He gradually became more fatigued and his legs much weaker. Two weeks before entry, after some light work, he was forced to go to bed. His cough increased and one week before entry he coughed up a slight amount of bright red blood with his sputum. He believed that his cyanosis had increased slightly during the past two weeks.

Physical examination was similar to that of his previous admission. The liver was felt two fingerbreadths below the right costal margin. There was slight clubbing of the fingers.

Examination of the blood showed a red cell count of 6,740,000, with a hemoglobin of 100 per cent and a white cell count of 6,700, 69 per cent polymorphonuclears. The oxygen capacity was 25.0 volumes per cent. The volume of the cells was 66.1 per cent. The volume index was 1.27, the color index 1.06. The vital capacity was 700 cubic centimeters. The nonprotein nitrogen of blood was 53 milligrams per cent; the serum protein 6.1 per cent.

His condition remained unchanged. He continued to have some bloody sputum. His skin was blue and almost black. X-ray examination of the chest showed slight fibrosis with no evidence of mediastinal tumor. He continued to fail gradually and died about two weeks after admission.

Differential Diagnosis

Dr. Francis M. Rackemann: "Five months before admission he again developed a chest cold, entered a hospital, and was told there that he had a blood disease." I assume that this blood disease was polycythemia. He came to the hospital with shortness of breath and with a marked bluish color all over. It is interesting to speculate a little. If it was a true polycythemia I think he should have been improved by the withdrawal of a pint of blood. Whatever it was he recovered all right. The shortness of breath continued but was not so severe. All this took place about five months before admission and during the interval he was working as a landscape gardener.

"He experienced cramps in the calves of his legs upon the slightest movement." I take it that that is a circulatory disturbance of the blood supply to his leg.

"The heart was not enlarged to percussion although the right border was 4 centimeters from the midsternal line." No doubt the heart borders were obscured by the tremendous emphysema.

The respirations were slow. Why were his respirations slow? Evidently because while lying in bed in no apparent distress, even in spite of his barrel-shaped chest and the evidence of emphysema, he was compensating at that moment and his breathing was easy.

The interesting feature in the physical examination at the second entry is that the liver was no farther down than two fingers, sometimes in emphysema it is down to the umbilicus. Clubbing of the fingers is also important. The record does not say whether the spleen was felt, as it might have been if the polycythemia was other than of the secondary type.

The oxygen capacity is above the normal. His blood was able to take up more oxygen than normal blood.

"The volume of the cells was 66.1 per cent. The volume index was 1.27." I take that to mean that the total volume of the blood cells was larger than normal: that all the cells together occupied a larger space and that each cell was a little larger in size than normal.

"The color index was 1.06." The cells contained a little more hemoglobin than normal.

It seems to me that this man with his story of trouble for about two and a half years undoubtedly has some sort of chronic infection in the chest which has led to the secondary formation of an emphysema and that he has a compensatory polycythemia, this time a quite marked grade; and then as time goes on the condition seems to get worse and eventually there is a terminal failure of the right heart and the picture of a typical cor pulmonale. That is the obvious explanation of this picture. We should not rest, however, without at least considering the matter of polycythemia, because the red count was so high. It seems to me that the absence of relief from bleeding and the absence of enlargement of the spleen would tend to rule that out. The question of mediastinal tumor has been considered but as a matter of fact cyanosis was generally distributed, in the feet as well as the head and hands; and x-ray of course ruled it out anyway. Beyond that I do not think of any other state that would come in.

I believe that Dr. Mallory will find this man with a very marked emphysema which I believe will be what he calls anatomical emphysema as well. I think the alveoli will be broken down. The patient raised blood on frequent occasions. That is evidence of coalescence of alveoli, and after it there will be thickening and evidence of congestion in the pulmonary circulation which in turn will cause a marked strain on the right side of his heart. I think that the sequence of events has occurred about in that order; that is, secondary infection first, emphysema second, polycythemia third, and strain on the heart fourth.

X-ray Interpretation

Dr. Aubrey O. Hampton: He had three or four x-ray examinations. At this first examination from that film alone we would be inclined to say the man had a big heart with passive congestion and some emphysema. There is nothing very startling in the anteroposterior view

of the chest. I think we would not know definitely from looking at that film whether he had asthma or not. If we had a fluoroscopic note to go along with it, we probably would. It is surprising how little you see in that film. The lateral view is quite a different picture. The anteroposterior diameter of the chest is greater than the transverse diameter and all the blood vessel markings show this queer separation in the substernal area which suggests blebs. In this oblique view you see little but this cavity-like formation along the margin of the sternum.

At the second examination you get a little more definite impression that the heart is enlarged. There is a dilated pulmonary artery. In the oblique view the pulmonary artery has pressed upon the esophagus so that we can say it is enlarged, and then working back, from this fact we can deduce that the strain was on the right side instead of the left side of the heart. He probably had right-sided enlargement of the heart. I do not see any other good reason for saying that. The question of fibrosis, which we had in the other cases, does not seem to come up here and we can say that this is an acute process at the right base, pneumonia or pneumonia plus passive congestion. This film here exaggerates the heart shadow and probably gives you a better idea of the right-sided heart enlargement than the other film. We have a high right auricular curve here. The trachea makes quite a bend toward the right. I had not noticed that. I do not know just why that is. It does not seem to be displaced here. I suppose that is the oblique projection which makes it look that way.

A Physician: I would like to ask about his blood Hinton. If the blood disease he had early were syphilis, I should think he might fit into the group of cardiac pulmonary sclerosis—so-called Ayerza's disease.

Dr. Tracy B. Mallory: I think it was negative, although I do not have the record.

Clinical Diagnoses

Asthma.
Emphysema.
Secondary polycythemia.
Cor pulmonale.

Dr. Francis M. Rackemann's Diagnoses

Asthma with secondary infection.
Emphysema.
Polycythemia.
Cor pulmonale.

Anatomic Diagnoses

Emphysema, diffuse.
Cor pulmonale.
Polycythemia.
Multiple petechial hemorrhages.
Chronic passive congestion of the liver and spleen.
Ascites, slight.
Cholesterosis of the gall bladder.

Pathologic Discussion

Dr. Mallory: This is a case that has left me completely puzzled. He had a very marked cor pulmonale, the heart weighing 550 grams. The right ventricle came right down to the apex of the heart and was distinctly larger than the left ventricle. He had, as Dr. Hampton pointed out, an extreme degree of barrel chest; that is, increase in the anteroposterior diameter. The diaphragm was flattened and low and the liver and spleen pushed down. They were also a little enlarged with chronic passive congestion, as you would expect with right-sided heart failure; but they were much lower than they were enlarged.

The lungs were extremely voluminous and I was particularly impressed with the way in which the apices crowded up into the suprasternal notch. On the autopsy table, when I first saw this man, I thought he certainly must have mediastinal tumor because at that time he showed intense congestion of the neck, face and arms, and none whatever of the lower half of the body, although cyanosis was previously noted on the ward in the lower half of the body. When we came to section these lungs, we could find very little emphysema in the sense of fusion of the alveoli. All the alveoli were uniformly dilated and possibly a little overdilated. I think one has to say there is a slight diffuse emphysema but it is not at all the striking picture that I think one might have expected.

The pulmonary artery showed no sclerosis whatever. All its main branches and its small branches were dilated and only here and there microscopically can we pick up a little bit of atheroma and intimal thickening. The pulmonary veins likewise were dilated. There was no scarring in the lung. The bronchi showed no hypertrophy of the muscle and were perfectly free from exudate. So that from the point of view of the autopsy we have a barrel chest, an early stage only of emphysema, but a very extreme grade of cor pulmonale such as you would expect only in the later stages of emphysema.

His bone marrow shows a very high grade of hyperplasia with an inversion of the normal ratio, ordinarily four white cells to one red. In this case the ratio is just about the reverse. It is perfectly consistent, however, with a secondary type of polycythemia, and I think that is probably what he had.

A Physician: Was the spleen big?

Dr. Mallory: It was about 300 grams. That is ordinarily just below the limit of palpability, not particularly large; and he had enough passive congestion of his liver to account for that much enlargement in the spleen also.

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NON-APPROVED MEDICAL SCHOOLS

IT is interesting to review the history of medical schools in America and to note certain trends and stages of development. In the Directory of the American Medical Association there is reference to over four hundred medical schools which have been chartered in what is now the United States. Of these, two date back to before the Revolution and three to before 1789. Although there has been a rapid decrease in the number of schools since 1910 to less than one hundred now in existence (including good, bad and indifferent) there was a far higher mortality in the last few years of the nineteenth and the early years of the twentieth century. Many of the schools were a mushroom growth, almost ephemeral, and to the shame of American medical education, one often finds the comment: "this school became fraudulent in its last years". It would throw light on one of the baser sides of American life to have, what cannot ever now be recorded, an accurate description of the rise and fall of these so-called medical schools.

Many of them were characterized as "proprietary", that is, they were operated for the benefit of a single proprietor or sometimes for a small group of owners. Their educational function was of slight importance, if any, and when the symbol of medical education, the medical degree was, as so often happens, mistaken for the reality of education itself, it became profitable to sell the degree without the education. The development of diploma mills in the United States was a marvelous growth difficult to understand after the lapse of years.

Such extensive hypocrisy and sham were bound to stir up reaction, and there developed fairly rapidly a sentiment in favor of protecting by governmental action under statute, the sick against the incompetent and the unscrupulous practitioners of the healing art. This double headed attack was only in part successful because the unscrupulous are not always technically incompetent, but very slowly public opinion has come to the support of measures calculated to eliminate the unqualified practitioner, whatever might be the cause of his disqualification.

Gradually organized bodies with varying degrees of authoritative opinion have given utterance to their judgments on medical schools, hoping that the force of public opinion would accomplish what could not be effected by statutory enactment. The charter of a medical school may be revoked for fraud but not for mere ignorance and incompetence on the part of the teaching staff.

If, however, the ignorance and incompetence are known, public opinion has an opportunity to work itself out. It is on this account that the so-called non-approved schools are so secretive about their inner workings. The results of their educational procedures are well known: their graduates are not well educated. Just how they actually carry on their work they refuse to disclose and they refuse to permit official evaluating bodies to make surveys.

Occasionally one of these schools has gotten into court, by compulsion of course, because although they make great show of bringing suit against persons or groups who attack them, the thought of actual court inquisition causes them great uneasiness. Then the court record of what they have actually done reads like opera bouffe, and several charters have been revoked for fraud.

In Massachusetts fifteen medical schools have been chartered. Of those which have endured to the present time, some have kept pace with progress and have been modernized. Some are still in the Dark Ages. Why should Massachu-

setts preserve one-third of all the medical schools not approved by the Council on Medical Education and Hospitals, in the United States?

THE ANNUAL MEETING OF THE MASSACHUSETTS MEDICAL SOCIETY

Section of Dermatology and Syphilology

The Massachusetts Medical Society proudly maintains that the *General Practitioner* is always the first in its mind. While its efforts for the medical profession are unending, it is at the Annual Meetings that this thought finds its best demonstration. Programs and exhibits are there for the visitor to hear and to see. The plans for the coming meeting at Springfield promise that this ideal of the Society will be fulfilled better than ever before. While the scientific aspects of medicine will not be forgotten, the papers will be designed to show the application of the art to practical medicine.

Among the programs which will be offered none will be more inviting to the general practitioner than that of the Section of Dermatology and Syphilology. The program, as planned, will be based on the everyday problems which the general practitioner is likely to meet at any time.

Every doctor frequently has to deal with a case of *syphilis*. There will be a paper on the better care of this disease, not only in the clinic but in the office, which will be read by a well-known syphilologist of one of our great hospitals. This paper will discuss wherein the average man fails in his methods and the path which he should follow.

A second paper will deal with the *Industrial Dermatoses*. This will be the special subject of this Section meeting. The speaker will be an international authority. He will consider these affections from all points of view in such a direct fashion that every doctor present will be better able to cope with the growing economic and medical problem of industrial disease.

A third paper will show the results of laboratory research combined with the practical work of the clinic and of practice in the diagnosis and treatment of mycotic disease. Not only will the reader discuss the comparatively familiar subject of external *mycotic disease,* but he will also deal with the little known topic of fungi as invaders of the internal organs. That these organisms may attack the lungs and other internal organs is a matter of such recent discovery that the average man may not yet have heard of the fact.

There will be other papers also, but all grouped around the needs of general medicine. Moreover, there will be a general discussion which will be open to everyone present.

CHIEF OF STAFF OF THE BOSTON SANATORIUM

Massachusetts occupies an enviable position in its treatment of the problems connected with tuberculosis. It has provided preventive and therapeutic measures for dealing with this disease on a large scale, having expended millions for hospitals, and has secured expert executives for the administration of its policies. Under her laws, municipalities have the option of maintaining hospitals for the treatment of cases of tuberculosis or utilizing county hospitals under specified rules and regulations.

Boston has for many years maintained a hospital for tuberculous patients in the Mattapan district which is now under the distinctive name of the Boston Sanatorium, a department of the Boston City Hospital.

The position of Chief-of-Staff is about to be filled and the appointment rests with the Trustees of the Boston City Hospital and approval of his Honor the Mayor. This is a part time position with a salary of $2500. Dr. Edwin A. Locke has held this position since the opening of the institution but has resigned.

This hospital is unusually well constructed and equipped with a bed capacity of about six hundred patients with a resident staff of five or six young men under the immediate supervision of Dr. Frank Hunt, resident physician, and Dr. Frederick L. Bogan, superintendent.

The position of Chief-of-Staff should require of this officer the determination of the medical policies of the institution. Unfortunately the management has not heretofore been accorded general approval and complaints and criticisms have been made, based on the suspicion of undue political interference. While this *Journal* is not possessed of specific facts, we are assured that the approval of the administration of this hospital has not been accorded by several well-known experts in this special medical field, in that adequate utilization of the voluminous material for study and teaching and the application of approved methods of treatment of this disease have been lacking.

It appears from statements made by one eminent expert that the whole institution and the good which it does for the city of Boston fade into insignificance as compared with the work in other similar institutions in New York City under the leadership of James Alexander Miller, Burns Amberson and Grant Thorburn; Benjamin Goldberg in Chicago and a similar group in Philadelphia.

The person to be selected as Chief-of-Staff of the Boston Sanatorium should be a physician who, by reason of an extended experience and recognized standing among his fellows, is known to possess the energy and qualities of leadership which will assure bringing the affairs of this

hospital to the important position expected of a department of the city of Boston.

The medical traditions of Massachusetts and Boston must be maintained in the appointment, if this community is to maintain its position in the profession. This means that politics must not enter into the selection of the person. Loyalty to the City and devotion to the care of victims of tuberculosis should inspire the appointment which is to be made.

We have in this city leaders in the scientific treatment of tuberculosis who would be glad to serve in this capacity. There is an opportunity for Boston doctors to see that the names of qualified persons are placed before the appointing body.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

PERKIN, H. J. B.S. University of Toronto. Research Fellow in Biochemistry, Lahey Clinic. Address: 605 Commonwealth Avenue, Boston. Associated with him is

LAHEY, FRANK H. M.D. Harvard University Medical School 1904. F.A.C.S. Director, Lahey Clinic. Surgeon-in-Chief, New England Baptist Hospital. Surgeon, New England Deaconess Hospital. Address: 605 Commonwealth Avenue, Boston. And

CATTELL, RICHARD B. A.B., M.D. Harvard University Medical School 1925. F.A.C.S. Surgeon, Lahey Clinic; New England Deaconess Hospital and New England Baptist Hospital. Address: 605 Commonwealth Avenue, Boston. Their subject is "Blood Iodine Studies in Relation to Thyroid Disease. Basic Concept of the Relation of Iodine to the Thyroid Gland; An Iodine Tolerance Test." Page 45.

LEONARD, EDWARD D. A.B., M.D. Harvard University Medical School 1913. F.A.C.S. Surgeon-in-Chief, Newton Hospital, Newton. Address: 129 Monadnock Road, Chestnut Hill, Mass. Associated with him is

DEROW, SIDNEY. M.D. Boston University School of Medicine 1930. Junior Surgeon, Newton Hospital, Newton. Address: 571 Commonwealth Avenue, Newton Centre, Mass. Their subject is "Mortality Factors in Acute Appendicitis. Study of 1,000 Cases." Page 52.

PREU, PAUL W. B.S., M.D. Cornell University Medical School 1930. Chief of Clinic, Psychiatric Clinic, New Haven (Conn.) Hospital. Associate Psychiatrist, New Haven Hospital. Instructor in Psychiatry, Yale University School of Medicine. Address: 333 Cedar Street, New Haven, Conn. Associated with him is

ROMANO, JOHN. B.S., M.D. Marquette University School of Medicine 1933. House Officer and Fellow in Psychiatry, Colorado Psychopathic Hospital, Denver, Colorado. Address: Colorado Psychopathic Hospital, Denver, Colorado. And

BROWN, WARREN T. M.D. University of Texas School of Medicine 1933. Resident in Psychiatry, New Haven (Conn.) Hospital. Instructor in Psychiatry, Yale University School of Medicine. Address: 333 Cedar Street, New Haven, Conn. Their subject is "Symptomatic Psychoses with Bromide Intoxication. Their Occurrence in Southern New England." Page 56.

O'KEEFE, EDWARD S. A.B., M.D. Harvard University Medical School 1911. Instructor in Pediatrics, Harvard University Medical School. Associate Pediatrician, Massachusetts General Hospital. His subject is "An Analysis of Three Hundred Cases of Asthma in Children." Page 62. Address: 31 Broad Street, Lynn, Mass.

TOWLE, HARVEY P. A.B., M.D. Harvard University Medical School 1892. Consultant in Dermatology, Massachusetts General Hospital. Address: 453 Marlborough Street, Boston. Associated with him is

GRUND, JACOB L. M.D. Harvard University Medical School 1921. Assistant Dermatologist, Department of Dermatology and Syphilology, Massachusetts Memorial Hospitals. Instructor in Dermatology and Syphilology, Boston University Medical School. Address: 483 Beacon Street, Boston. Their subject is "Progress in Dermatology, 1935." Page 65.

CORRECTED STATEMENT OF THE POSITIONS OCCUPIED BY DR. TIMOTHY LEARY

LEARY, TIMOTHY. A.M., M.D. Harvard University Medical School 1895. Medical Examiner, Suffolk County. Professor of Pathology Emeritus in Tufts College. His subject was "The Death Rate from Alcoholism." Page 15, issue of January 2.

Address: 784 Massachusetts Avenue, Boston.

The Massachusetts Medical Society

SECTION OF OBSTETRICS AND GYNECOLOGY*

C. J. KICKHAM, M.D., *Chairman*, 524 Commonwealth Ave., Boston, Mass.
R. S. TITUS, M.D., *Secretary*, 472 Commonwealth Ave., Boston, Mass.

BLEEDING IN PREGNANCY

Vaginal bleeding during pregnancy must always be considered abnormal. It will usually be due to one of the following causes: threatened abortion, or miscarriage, lesions of the

*A series of short selected articles by members of the Section is being published weekly.
Comments and questions by subscribers are solicited and will be discussed by members of the Section.

cervix, ectopic pregnancy, placenta praevia, separation of the placenta, hydatidiform mole, or the onset of labor. Most of these conditions will be treated in detail in subsequent papers. The present discussion is intended as a general introduction to the problem.

When any bleeding occurs in a patient who is known to be, or might be, pregnant, the first consideration is the duration of the pregnancy. If the patient is five months or more pregnant there is always the possibility of a placenta praevia or a separation of the placenta. Erosions of the cervix and cervical polyps may be the cause of slight bleeding and the onset of labor is often accompanied or preceded by bloody show. Such cases need not always be immediately investigated to determine the presence or absence of a placenta praevia but they ought always to be regarded with suspicion until the cause of the bleeding is determined. The cervix is seldom the source of profuse or persistent bleeding and when such occurs in the latter half of pregnancy it usually means separation either of the normally implanted placenta or of a placenta praevia. The special problems connected with these complications will be taken up later and the remainder of our discussion will be concerned only with bleeding before the fifth month.

BLEEDING BEFORE THE FIFTH MONTH OF PREGNANCY

In order to avoid mistakes and delays in diagnosis it is wise to regard any bleeding which begins several days after the date a period was expected as possibly a complication of pregnancy until it becomes clear that it is merely delayed menstruation. This is particularly true when there is anything about the bleeding which is not usually characteristic of the patient's periods, such as, for instance, scanty or intermittent flow, unusual pain, unusual duration, or the passage of clots. The bleeding may vary in amount from a few drops to a serious hemorrhage. Bleeding profuse enough to be itself a threat to the patient demands immediate investigation by vaginal examination and since such an amount of bleeding is usually due to beginning abortion, preparations should be at hand for curettage, packing of cervix and uterus, and the possible need of transfusion should be foreseen. Not infrequently, of course, the history, the amount of bleeding, the passage of clots or portions of the ovum, or the occurrence of uterine cramps make it obvious at once that the case is one of inevitable or incomplete abortion.

More commonly, however, the bleeding is moderate or slight in amount and the patient is not definitely aborting. In such cases the first question should be whether the patient is known to have, or may reasonably be presumed to have, an intrauterine pregnancy. If the patient has been examined previously and the diagnosis of intrauterine pregnancy made, the possibility of ectopic pregnancy is almost excluded. It ought, however, to be remembered that rarely ectopic and intrauterine pregnancies occur coincidentally in the same patient. If the patient has never been seen before but shows on rectal examination or abdominal palpation a definitely enlarged uterus, it is reasonable to assume for the time being that she has an intrauterine pregnancy.

On the other hand, if there is doubt about the existence of an intrauterine pregnancy, one should always think of the possibility of ectopic pregnancy. If pelvic pain is a conspicuous symptom or there is a history of recent attacks of pelvic pain, immediate vaginal examination is advisable and should be done under anesthesia if inconclusive without anesthesia. It is well to remember that the pain and bleeding of an early tubal pregnancy may closely simulate the onset of an abortion.

When there is moderate bleeding and no question of ectopic pregnancy arises, the sensible assumption is that the bleeding is due to slight separation of the ovum, i.e., that abortion is threatened. Vaginal examination should, therefore, be deferred until the bleeding has stopped or until the persistence of bleeding, or an increase in its amount, makes examination imperative. When the deferred examination is made, it will sometimes be found in cases of slight bleeding that a cervical lesion is the cause.

Subsequent papers will take up in detail ectopic pregnancy, threatened abortion and lesions of the cervix.

MASSACHUSETTS LEGISLATIVE NOTES

The Special Commission on Public Health Laws and Policies has submitted the following preliminary report:

"Owing to the many details necessary to develop and perfect plans for the study committees, the formal completion of organization was not effected until September 9, 1935, at which time the Commission met and elected the following: Dr. Henry D. Chadwick, Chairman; Dr. Wilson G. Smillie, Vice Chairman; Dr. Charles F. Wilinsky, Secretary-Treasurer.

"An executive committee was appointed, composed of the above-mentioned officers together with Dr. Alexander S. Begg, Prof. Curtis M. Hilliard, Dr. Charles E. Mongan and Dr. Winfred Overholser.

"The Commission appointed fourteen committees to study major public health problems and procedures. Each committee has in its membership at least one member of the Commission. The several committees are composed of leaders throughout the State in their respective fields. The subjects being studied by these fourteen committees are (1) Codification of public health laws, (2) Pub-

lic health practices and procedures, (3) Acute communicable disease control, (4) Public sanitation, (5) Maternal and infant hygiene, (6) Child hygiene, (7) Social hygiene and gonorrhea and syphilis control, (8) Hospitals, dispensaries, clinics and health centers for medical service to indigents, (9) Mental hygiene, (10) Tuberculosis control, (11) Occupational hygiene, (12) Adult hygiene and special medical problems, such as cancer, chronic rheumatism, diabetes and heart disease, (13) Public health nursing, and (14) Dentistry and oral hygiene.

"These committees have organized, formed subcommittees, and are busily engaged in the study of their respective problems. More than one hundred men and women, specialists in their respective fields, are giving freely a great deal of time and effort to the work of the Commission. The enthusiasm with which these leaders are attacking their problems is most gratifying and augurs well for a truly comprehensive and well-conceived report. Over forty meetings have already been held.

"Owing to the fact that it was impossible to organize the Commission until September and to effectively launch its comprehensive program until late in October, it obviously cannot complete its work as specified in the resolve by the first Wednesday in December.

"Confident that such recommendations as are under consideration by the Commission will greatly strengthen the effectiveness of public health work in the Commonwealth, it is recommended that an extension of time be granted for completion of its work not later than the first Wednesday in December, 1936."

S. 24. On petition of Joseph A. Langone, Jr., this bill seeks to have the boards of trustees of the institutions in the Departments of Mental Diseases and Public Welfare abolished and the powers and duties of such trustees transferred to the Governor and Council.

H. 36. The especially important recommendation in this bill is that of the Commissioner of Mental Diseases to have Section 4 enacted. This reads as follows:

"In view of the frequency with which psychiatrists appear in cases coming before the courts, and particularly the criminal courts, and in view of the criticisms sometimes made relative to the testimony of unqualified persons who hold themselves out to be experts in mental disease, it seems only proper that some minimum qualifications should be recognized in the law. The proposed bill sets up requirements which may be considered as the minimum which should be expected of a psychiatrist who purports to qualify as an expert in mental diseases."

H. 35, providing for the annual registration of physicians, has already been published in this *Journal*. See page 1206, issue of December 12, 1935.

H. 34. This is the other bill submitted by the Board of Registration in Medicine which provides for methods for raising the standards of medical education. This bill has been published in this *Journal*. See "Proposed Amendment to the Massachusetts Statute Relating to the Registration of Physicians." Page 937, issue of November 7, 1935.

H. 59. This bill seeks to have defined the term *stillborn* in the following language: A stillborn child shall be deemed to be a foetus born after a period of gestation of not less than five months, in which foetus there is no attempt at respiration, no action of heart and no movement of voluntary muscle.

H. 46. The purpose of this bill is to change the name of the State Infirmary to State General Hospital.

H. 167. On June 26, 1935 a Resolve, providing for an Investigation by a Special Commission relative to the Advisability of establishing a System of Public Clinics, Hospitals or Other Establishments for the Treatment of Persons addicted to Gross and Confined Habits of Intoxication, was passed.

The Commission has submitted its report which consists, first, of a report of a hearing; secondly, a discussion of the problems connected with the use of alcohol, and thirdly, certain recommendations.

This is a remarkable document and warrants careful study in that it gives to the citizens of the Commonwealth a history of the state activities in dealing with alcoholism, facts relating to inebriety and the conclusions of the Commission as follows:

"Although it is not strictly within the purview of this Commission, it would seem timely to point out here that a fundamental attack upon the problem of alcoholism involves, first, a long campaign of education concerning the untoward effects of alcohol,—a campaign which was very largely dropped at the time the prohibition amendment was enacted. Further than this, a stricter control of the sale of alcohol seems urgently indicated. This has worked successfully in England and Germany, by the limitation of hours during which the drinking places may be kept open, and by a heavy tax on spirituous liquors which would tend to force indulgence away from that group toward the group of light wines and beer, which are considerably less harmful from the medical point of view. It was argued before the committee of the General Court which heard the original bill, as a result of which this Commission was established, that at the present time this country is faced with a younger generation which is largely ignorant of the evil effects of alcohol, and which, through the public psychology which arose during the prohibition era, considers it rather 'smart' to become intoxicated. That a certain measure of justice and truth exists in this statement cannot be denied, even though the slight decrease in the number of arrests for drunkenness during the current year may offer some hope for the future.

"The principal disadvantage of the present provision for the civil commitment of inebriates, and drug addicts for that matter, is that even though

the commitment is civil it must be made to a penal institution,—namely, the State Farm in the case of men, and the Reformatory for Women in the case of women. An additional handicap exists in the fact that although a criminal commitment for drunkenness to the State Farm calls for a maximum of one year, a civil commitment to the same institution by reason of inebriety provides for a maximum of two years.

"It would be entirely logical for the General Court to authorize the care of the inebriates by the Department of Mental Diseases, as was the case prior to 1922. The mental hospitals of the State are, however, at the present time crowded, with an average overcrowding of slightly over 17 per cent, and an annual net increase of about 460 patients under care is to be expected. Should the General Court, therefore, consider this change advisable it would be necessary to provide suitable buildings which should be located on the grounds of some institution with a large land area, as, for instance, the Gardner State Hospital, so that the patients committed could be kept separate from the insane and have an ample opportunity to work out of doors. The proper size of such facilities is entirely problematical; it seems clear, however, from the history of Foxborough and Norfolk experiments, that a separate institution is not warranted. On October 31, 1935, for example, there were only 17 male inebriates under commitment at the State Farm, and only 7 women at the Reformatory for Women. Although it is reasonable to suppose that some increase might be expected if commitments could be made to a hospital instead of to a correctional institution, there seems to be some reluctance on the part of the court to make use of the existing provisions of civil commitment. Unless and until the General Court finds it feasible to establish suitable facilities at some existing state hospital, no change in the existing law is recommended by your Commission.

"Arthur T. Lyman,
Winfred Overholser,
Henry D. Chadwick."

MISCELLANY

AFFAIRS OF THE ACADEMY OF PHYSICAL MEDICINE

Dr. Franklin P. Lowry of Newton was elected Secretary-Treasurer of the Academy of Physical Medicine recently by the Directors to fill the unexpired term of the late Dr. Arthur H. Ring, who had held that office from 1931 to the time of his death.

Boston has been selected as the place for the Annual Meeting in October 1936. The Academy met last in Boston in 1930.

Members of the Program Committee for the Boston meeting are as follows: Dr. William D. McFee, Boston, Chairman; Dr. William Bierman, New York City; Dr. Ralph Pemberton, Philadelphia; Dr. Grant E. Ward, Baltimore; Dr. George Miller MacKee, New York City; Dr. Francis P. McCarthy, Boston; Dr. Groesbeck F. Walsh, Fairfield, Alabama.

CORRESPONDENCE

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

535 North Dearborn Street, Chicago, Ill.,
December 30, 1935.

Managing Editor, *The New England Journal of Medicine,*

In addition to the articles enumerated in our letter of December 4 the following have been accepted:

Lederle Laboratories
Antidysenteric Serum (Polyvalent) 20 cc. vial package

Parke, Davis & Co.
Mapharsen
Ampoules Mapharsen 0.04 Gm.
Ampoules Mapharsen 0.06 Gm.
Ampoules Mapharsen 0.4 Gm.
Ampoules Mapharsen 0.6 Gm.

E. R. Squibb & Sons
Squibb Cod-Halibut Liver Oil

Winthrop Chemical Co. Inc.
Ampules Suprarenin Powder, 0.05 Gm.

The following product has been accepted for inclusion in the List of Articles and Brands Accepted by the Council But Not Described in N.N.R. (New and Nonofficial Remedies, 1935, p. 445):

The National Drug Co.
Smallpox Vaccine (Vaccine Virus)

Paul Nicholas Leech, *Secretary,*
Council on Pharmacy and Chemistry.

RECENT DEATHS

MITCHELL—Winthrop Dodd Mitchell, M.D., a retired surgeon, died at his home in Worcester, Massachusetts, December 30, 1935. He was born in East Orange, New Jersey, in 1862, the son of Aaron Peck Mitchell and Elizabeth (Dodd) Mitchell and was educated at Phillips (Andover) Academy and graduated in medicine from the Bellevue Hospital Medical College in 1887. He later studied in Vienna, Munich and Dublin.

He was formerly associated with several New Jersey hospitals, having served as Medical Director Emeritus of St. Michael's Hospital, Newark, New Jersey.

He was a Fellow of the American College of Surgeons, a member of the Worcester Club and the Tatnuck Country Club of Worcester.

A widow and a daughter survive him.

MURPHY—TIMOTHY JOSEPH MURPHY, M.D., LL.D., of 372 Dudley Street, Roxbury, whose office was at 520 Beacon Street, Boston, died January 1, 1936, after a short illness.

He was born in 1866. Early in life Dr. Murphy was a reporter on *The Boston Herald*. After graduating from Boston College in 1888 he entered the Harvard Medical School and was given his M.D. degree in 1892.

He was chief of staff of Boston Sanatorium, Professor of Medicine at Tufts College Medical School and member of the Staff of St. Margaret's Hospital, and had served as President and Censor of the Norfolk District Medical Society.

Dr. Murphy belonged to the Catholic Alumni Society, the Massachusetts Order of Foresters and Knights of Columbus.

He was recently appointed Medical Examiner of the M. C. O. F. In addition to the Massachusetts Medical Society, Dr. Murphy was a Fellow of the American Medical Association.

Six children survive him.

MORRIS—GEORGE PATRICK MORRIS, M.D., of 811 Broadway, South Boston, died January 4, 1936, after a long illness. He was born in 1860. After his preliminary education at the Boston Latin School, Dr. Morris entered Harvard College graduating therefrom in 1883 and from the Medical School in 1891.

He was a member of the South Boston Medical Society and a Fellow of the Massachusetts Medical Society and the American Medical Association.

Dr. Morris is survived by his widow, Mrs. Katherine J. Morris; a son, George P. Morris; two daughters, Miss Mary G. Morris and Miss Eleanor L. Morris; two sisters, Miss Mary T. Morris and Miss Agnes C. Morris, and two brothers, Mr. Robert E. Morris and Mr. Charles H. Morris.

NOTICES

A LECTURE BY DR. E. V. McCOLLUM

The Worcester County Home Economics Association is sponsoring a lecture by Dr. E. V. McCollum, Ph.D., Sc.D., the noted research worker, author and lecturer at Johns Hopkins University, on Friday evening, January 17, at the Worcester Girls' Trade School, High Street, Worcester. His subject will be Nutrition in Its Newest Phase. Tickets are seventy-five cents and may be obtained at Easton's, 426 Main Street, Worcester, on or after January 10.

BOSTON DISPENSARY

25 Bennet Street, Boston
Medical Conference Program
9-10 A.M., January, 1936

Thursday, January 9 — G. I. Clinic. Dr. K. S. Andrews.

Friday, January 10—Recent Studies of Internal Secretion. Dr. Joseph C. Aub.

Saturday, January 11—Presentation of Ward Cases. Dr. Jacob Schloss.

Tuesday, January 14—Cases from Blood Clinic. Dr. Isadore Olef.

Wednesday, January 15 — Modification of History Taking and Physical Examination Methods in Pediatrics. Dr. Francis McDonald.

Thursday, January 16—Social Service Case Presentation. Miss Edith Canterbury.

Friday, January 17—The Diagnosis and Management of Biliary Tract Disease. Dr. Frank H. Lahey.

Saturday, January 18—Presentation of Ward Cases. Dr. H. C. Gordonier.

Tuesday, January 21 — Diagnosis of Polycythemia. Dr. William Dameshek.

Wednesday, January 22 — Some of the Newer Aspects of Cancer. Dr. William M. Shedden.

Thursday, January 23—Allergy Clinic. Dr. Joseph Kaplan.

Friday, January 24 — Some Aspects of Hemolytic Streptococcal Infection. Dr. Chester S. Keefer.

Saturday, January 25—Presentation of Ward Cases. Dr. Heinz Magendantz.

Tuesday, January 28 — X-ray Demonstration. Dr. Alice Ettinger.

Wednesday, January 29—Pediatric Case Presentation. Dr. Francis McDonald.

Thursday, January 30 — Case Histories in Brain Tumors. Dr. J. J. Skirball.

Friday, January 31—The Heart and Aorta in Chronic Hypertension. Dr. Paul Dudley White.

MEDICAL CLINIC AND STAFF ROUNDS AT THE PETER BENT BRIGHAM HOSPITAL

At 3:30 P.M. on Thursday, January 16, in the Amphitheatre of the Peter Bent Brigham Hospital, Dr. Henry A. Christian, Physician-in-Chief, Hersey Professor of the Theory and Practice of Physic in the Harvard Medical School, will give a medical clinic. To it are cordially invited practitioners and medical students.

On Saturdays in the wards of the Peter Bent Brigham Hospital, from 10 to 12, staff rounds will be conducted by Dr. Christian.

LAWRENCE CANCER CLINIC

Established 1928

Lawrence, Mass.,
December 30, 1935.

To the Physicians of the North Half of Essex County:

Dear Doctor:

The regular Lawrence Cancer Clinic, to be held at Lawrence General Hospital, 1 Garden Street, Lawrence, upon Tuesday, January 21, at 10:00 A.M., will be a Demonstration Clinic with Channing C. Simmons, M.D., of Boston, Associate in Surgery in the Graduate Courses in Medicine at Harvard University Medical School, Surgeon-in-Chief to Collis P. Huntington Memorial Hospital, member of the Cancer Commission of Harvard University and Visiting Surgeon to Massachusetts General Hospital, Boston, present as consultant. You are invited to

accompany any of your patients whom you desire shall have this service, or to send them with a note, and a report will be returned to you. The service is gratis. Your attendance at the Clinic is always welcome.

This Clinic is endorsed by the Committee on Postgraduate Instruction of the Massachusetts Medical Society.

Committee
ROY V. BAKETEL, M.D.,
CHAS. J. BURGESS, M.D.,
FRED'K D. MCALLISTER, M.D.,
JOHN J. MCARDLE, M.D.,
HARRY H. NEVERS, M.D.,
THOS. V. UNIAC, M.D.,
J. FORREST BURNHAM, M.D., *Chairman.*

REPORTS AND NOTICES OF MEETINGS

HARVARD MEDICAL SOCIETY

The Harvard Medical Society met at the Peter Bent Brigham Hospital November 26, with Dr. Henry A. Christian presiding. The first case was presented by Dr. Lawrence E. Putnam of the medical service: A twenty-nine year old native housewife entered one and a half weeks previously with the complaint of a cough of six weeks' duration. Between the ages of ten and fourteen years she was in a tuberculosis preventorium, because of a definite family history of tuberculosis. Between the ages of fourteen and nineteen years she lived with an aunt and three sisters. The latter have since developed active pulmonary tuberculosis. Her father and one other sister had had pulmonary tuberculosis. At the age of twenty-three years she suffered a "chest cold", with pleuritic pain in the right chest, and had afternoon fever as high as 102 degrees Fahrenheit. She stayed in a tuberculosis sanatorium for six months at that time. Five years ago at the age of twenty-four years she was married, and has since had two children without ill event or reactivation of the pulmonary disease. Six months ago an x-ray of the chest is said to have shown a "scar at the right apex". Six weeks before entry she developed pleuritic pain in the left lower chest, and one week before entry began to experience night sweats. On admission she had severe cough, dyspnea, and vomiting. Physical examination on entry was negative except for the lungs. There was dullness at both apices, greater on the right, and dullness in the left axilla and left chest anteriorly. There were numerous medium moist râles and diminished breath sounds over these areas. Urinalyses were negative. The hemoglobin was 85 per cent, the red blood count 3,900,000 to 4,500,000, and the white count 9,000 to 12,000 with 10 per cent monocytes. Four sputum examinations were positive for acid-fast organisms. For the first three days after entry her temperature rose to ninety-nine degrees in the afternoon; since that time it had been normal. X-ray plates taken the day after entry showed consolidation at the right apex, interpreted as tuberculosis, and a uniform consolidation at the left base, which was interpreted as bronchopneumonia. One week later the roentgenological picture remained the same, and the consolidation at the left base was interpreted as probably being of tuberculous nature.

Dr. Christian commented on the fact that some six months ago x-ray studies had shown an apparently healed process, and that at recent examinations large numbers of tubercle bacilli had been found in the sputum. He raised the questions as to whether the apical or basal lesion was the source of the organisms, and what the significance of the basal lesion might be.

Dr. Burgess Gordon spoke of the striking absence of signs of toxicity in this case. Many cases of tuberculosis with basal lesions have no symptoms except those suggesting pleurisy or bronchiectasis. They usually do not produce a positive sputum until late in the disease process.

Dr. Lowrey F. Davenport remarked on the change of attitude relative to pregnancy in tuberculous women. It is the present consensus that it is not the pregnancy itself, but the increased physical activity in the home during the first six months after delivery that is responsible for aggravating the infection. The advisability of aborting such women is now regarded with more conservatism than formerly.

Dr. Robert Bates presented the surgical case: A forty-nine year old married male cabinetworker, who was admitted to the hospital from Middlesex sanatorium for thoracoplasty. In 1914 he had had pleurisy on the right side. In 1917 he experienced hemoptysis and weight loss. In 1922 he suffered gross pulmonary hemorrhage, and was treated in the Rutland Sanatorium. Since that time he had numerous hemoptyses and hospitalizations. On admission to the Peter Bent Brigham Hospital he had an advanced fibrocaseous tuberculosis of the upper half of the right lung, with minimal lesions at the left apex. A two-stage thoracoplasty was performed on the right side, with the removal of the first nine ribs. Dr. Harlan F. Newton remarked on the fact that the patient had been treated for eleven years without active collapse therapy. The extent of the active process in the right lung without more involvement of the left is striking, and surgical measures must be approached carefully in such cases because of the danger of initiating a tuberculous pneumonia in the good lung. Dr. Elliott Cutler raised the question whether such patients who are obviously a menace to society cannot be confined to sanatoria until their disease is at least quiescent. Dr. Christian replied that the state had no such power over tuberculous patients.

Dr. Christian introduced Dr. Burgess Gordon, a former resident on the medical service at the Peter Bent Brigham Hospital, and at present associate professor of medicine at Jefferson Medical College; physician in charge of the department of chest diseases of the Jefferson Hospital, and visiting physi-

cian in the Pennsylvania Hospital. Dr. Gordon spoke on the "Mechanics and Effects of Abdominal Compression in the Treatment of Pulmonary Tuberculosis". His paper will be published in an early issue of this Journal.

Dr. E. S. Emery, Jr., in commenting on the paper, remarked that the vital capacity and diaphragmatic excursion was less in athletes than in non-athletes, and questioned whether the vital capacity was a reliable measure of the pulmonary efficiency in any condition except cardiac disease.

Dr. Harlan F. Newton stated that it was not the height of the diaphragm, but the elimination of its pumping motion that was of importance in explaining whatever benefit might be derived from diaphragm immobilization.

FAULKNER HOSPITAL CLINICAL MEETING

The regular monthly clinical meeting was held at the Faulkner Hospital on January 2 at 5:00 P.M.

One of the cases which came to autopsy during the preceding month was presented. This brought out several points of interest. The patient had chronic tuberculosis of the apices and tuberculous lesions in the cecum. During the World War this patient had had attacks of "dysentery", and the question immediately arose whether the dysentery at that time could have been due to tuberculous lesions. Apparently even at autopsy it is difficult to decide just how old tuberculous lesions are. This is an important point in regard to the question of compensation from the government. The next point was the fact that it is so difficult to find tuberculous bacilli in the spinal fluid. It is, of course, possible that in cases where there is an increased cell count and a pellicle formation there are no organisms in the spinal fluid but the reaction in the spinal fluid is the result of the lesions and organisms in the meninges. This patient turned out to have miliary tuberculosis and the lesions in the meninges were miliary tubercles. A most exhaustive search was made of several specimens of the spinal fluid, and although a pellicle developed in some of the specimens, no organisms were found. Another interesting point in this case was the clearing up of the spinal fluid by constant drainage. A needle was inserted into the spinal canal in the lumbar region and left there for four days, while constant intravenous salt solution was given. The cell count in the spinal fluid diminished considerably during this drainage, but as there was a diffuse miliary tuberculosis the patient naturally did not improve.

The next case reported was a patient with thrombocytopenic purpura in which the outstanding symptom was pronounced flowing from the uterine mucosa. It was felt at first that the case was one of some disturbance of the hormone of the anterior part of the pituitary gland. Eventually hemorrhage from the gastric mucosa developed and generalized purpura. The possibility of both conditions being present was considered. The blood platelets became less and less in the blood and after the fourth transfusion disappeared quickly suggesting that some destructive process for blood platelets was active in the body. Hemorrhage eventually developed in one of the eyegrounds. The spleen was removed and during the three weeks after splenectomy no transfusions were needed and the red blood count returned to 4,500,000. The pathologist emphasized the fact that there is no definite pathology peculiar to this condition existing in the spleen. In the spleen from this particular case there was phagocytosis of erythrocytes and marked hyperplasia of the endothelial cells in the center of the lymph follicles and also enlargement of the lymph follicles. The therapeutic effect of splenectomy in these cases is one of the dramatic cures in medicine.

Dr. Maurice B. Strauss then gave an excellent presentation of his work on anemias in pregnancy. He called attention to the fact that a Boston physician, Dr. Walter Channing, was one of the first, ninety-five years ago, to mention anemias in pregnancy. Dr. Strauss called attention to the fact that he was talking about a series of cases in which obvious causes for anemia were absent. In two thousand cases in which obvious causes for anemia did not exist, 50 per cent of the cases showed a hemoglobin below 70 per cent. In this group the so-called ward cases showed a higher incidence than private cases. No apparent cause for the anemia is found. It is spoken of as hypochromic anemia and is looked upon as due to a deficiency in iron. Three possibilities present themselves:

1. Inadequate iron in the diet.
2. Gastric anacidity or some defect in the secretion of the stomach which effects the assimilation of iron.
3. Loss of iron.

He showed that in some cases the acidity in the gastric juice gradually diminished as pregnancy proceeded and in the cases in which the acidity was lessened there usually was more loss of hemoglobin. The diet of these patients is apparently a factor. A good diet consists of meat and vegetables. In patients in whom the diet was not especially rich in meat and vegetables, there was more anemia. It is interesting to note that in these cases pallor is not a pronounced symptom. Under the microscope the red blood cells are usually smaller than normal, have some change in shape but little change in size and there is distinct achromia. He showed charts to emphasize the fact that, despite the anemia in the mother, practically all the babies are born with the same amount of hemoglobin and are not anemic at birth.

The treatment of this condition consists of iron in adequate amounts. The type of iron administered is not important but it is essential to see that enough is absorbed to accomplish the results. Ferrous salts are more effective than ferric salts and therefore it is important to see that the iron is not oxidized. Most pharmaceutical houses arrange

their preparations so that oxidation does not take place.

Occasionally an anemia is spoken of as macrocytic anemia, which is similar to pernicious anemia and occurs in pregnancy but this is very rare. This anemia is apparently due to a lack of an intrinsic factor in the gastric juice which is essential to prevent primary anemia or a lack of the liver factor in the diet, or an inability to absorb this factor. In the few cases of macrocytic anemia which have been observed in Boston, it is felt that the cause is due to a lowering of the intrinsic factor in the gastric juice rather than to a disturbance in absorption or a lack of the liver element in the diet. Some comparison has been made with cases in India in which a lack of the liver element in the diet is the important factor. Apparently in certain cases the intrinsic factor in the gastric juice, which is important in anemia, may temporarily diminish in pregnancy. This type of anemia should be treated with liver extract and usually the liver extract can be stopped after the blood has returned to normal. Transfusions are not indicated unless the anemia has reached such a severe grade that it becomes a temporary emergency.

Another interesting observation was the fact that babies of untreated anemic mothers tended to be anemic at the end of a year, while babies of mothers who are not anemic and babies of mothers who were anemic but were treated did not show anemia at the end of a year.

ALPHA OMEGA ALPHA LECTURE

The first Alpha Omega Alpha Lecture of the current academic year was delivered at the Harvard Medical School December 12, 1935, by Dr. Warfield T. Longcope, Professor of Medicine at the Johns Hopkins University Medical School, who spoke on "Studies in the Natural History of Bright's Disease."

Bright's disease must be considered as a general systemic disease, in which the renal lesions are but a part of the many manifestations. The renal involvement may be considered analogous to the involvement of the heart in such diseases as rheumatic fever and syphilis. Acute hemorrhagic nephritis was selected for study with the hope of clarifying its etiology and pathogenesis.

At least 90 per cent of the cases of acute hemorrhagic nephritis follow infections with hemolytic streptococci, and recent work has shown that the majority of these cases occur after infections caused by the beta, or minute form of the organism. The mode of action of these bacteria in producing the disease has been investigated by many workers. Acute glomerular reactions have been produced in animals by injections of the toxins of hemolytic streptococci, and by severe peritoneal infections with the same organism. Pappenheimer sensitized animals to streptococcal proteins, and subsequently injected the dead bacteria into the renal artery, with the production of acute glomerular lesions, which appeared identical microscopically with those of acute glomerular nephritis. Dr. Longcope obtained similar results with injections of Streptococcus viridans, the lesions produced being more diffuse and extensive than those obtained from injections of Streptococcus hemolyticus. Only certain strains of each group were effective, however.

Of the 125 cases investigated by Dr. Longcope, a characteristic prodromal period followed the acute infection before the onset of the nephritis. This period varied from three to twenty-eight days, and eighty per cent of the cases appeared between the seventh and sixteenth days.

Although acute hemorrhagic nephritis resembles rheumatic fever in appearing after infection with beta hemolytic streptococcus, there are several important differences between the pathogenesis and epidemiology of the two diseases. The primary infection in acute glomerular nephritis unlike rheumatic fever is not always confined to the respiratory tract, since cases have been observed following impetigo, erysipelas, and wound infections. The variation between the climatic distributions of the two diseases is quite striking, for whereas the incidence of rheumatic fever falls progressively from the cold climates of the north to the semitropical climates of the south, the incidence of acute glomerular nephritis is practically identical in the two areas. Rheumatic fever is prone to undergo exacerbations, while acute glomerular nephritis once cured does not recur.

Careful study of fatal cases has shown that the majority of fatalities are characterized by an insidious onset following subacute recurring infections (e.g., infected sinuses) of streptococcal etiology. Such cases may show edema and albuminuria, and gradually develop marked and persistent elevation of the blood pressure. They proceed with a subacute course, and recurrence of edema, fever, and hematuria with each flare-up of infection.

These findings have led Dr. Longcope to consider that there are two types of hemorrhagic glomerular nephritis, each with a characteristic clinical course and termination. The first type is characterized by an abrupt onset, an acute course, and usually terminates with healing. The second has an insidious onset, subacute course with remissions and exacerbations, and frequently terminates fatally. There is some question as to whether the latter type is due to streptococcal infection. It is true that pneumococcal infections are able to produce this type of disease.

Patients with the acute form show a high titer of antistreptolysins in the blood serum following acute infections. Patients with the subacute, progressive form of the disease have a persistent low titer. The former group shows a good skin reaction to filtrates or proteins of the bacteria, in contrast to the latter group, which only rarely shows such a reaction.

Thus the two forms may be considered as infectious diseases, in which the reaction of the individ-

ual to the infection is different. The antibody reaction power of the patient of the first class is highly active, but is suppressed or absent in the subacute group.

Treatment of acute hemorrhagic nephritis must be based on the fundamental principles of treatment of any acute infection involving a vital organ. Special attention must be paid to eradicating the seat of focal infection.

SOUTH END MEDICAL CLUB

The next regular meeting of the South End Medical Club will be held at the office of the Boston Tuberculosis Association, 554 Columbus Avenue, Boston, on Tuesday, January 21, at 12 noon. The speaker will be James W. Manary, M.D., Superintendent and Medical Director of the Boston City Hospital. His subject will be "The Growth of Dispensary Service at the Boston City Hospital." All physicians are cordially invited to attend this meeting. The usual luncheon will be served.

THE AMERICAN COLLEGE OF PHYSICIANS

The Twentieth Annual Session of the American College of Physicians will be held in Detroit with headquarters at the Book-Cadillac Hotel, March 2-6, 1936.

Dr. James Alex. Miller of New York City, is President of the College, and has arranged a program of general scientific sessions of great interest to those engaged in the practice of Internal Medicine and associated specialties. Dr. Charles G. Jennings, of Detroit, is the General Chairman of the Session, and is in charge of the program of clinics and demonstrations in the hospitals, medical schools and other Detroit institutions. Dr. James D. Bruce, Vice-President in Charge of University Relations, University of Michigan, is Vice-Chairman of the Committee on Arrangements, and has in charge the preparation of an all-day program to be conducted at the University of Michigan on Wednesday, March 4. Dr. Walter B. Cannon, Professor of Physiology at Harvard University Medical School, will deliver the annual Convocation Oration on "The Rôle of Emotion in Disease." Dr. Miller's presidential address will be on "The Changing Order in Medicine." About fifty eminent authorities will present papers at the general scientific sessions, while clinics and demonstrations will be conducted at the Harper, Receiving, Ford, Grace, Herman Kiefer and Children's Hospitals, of Detroit.

NEW ENGLAND PHYSICAL THERAPY SOCIETY

The regular meeting of the New England Physical Therapy Society will be held at the Hotel Kenmore, Boston, on Wednesday evening, January 15, 1936, at 8 P.M.

PROGRAM

Hyperesthetic Rhinitis and Its Treatment (Illustrated). The Modern Treatment of the Common Cold. George B. Rice, M.D., Boston.

The discussion will be led by Leighton F. Johnson, M.D., Boston.

The Progress Committee will submit a report on evaluation and progress in the field of short wave therapy by DeWitt G. Wilcox, M.D., of Newton and William D. McFee, M.D., of Boston.

The Council will meet at six.

Members and guests will meet at dinner in the main dining room of the Hotel Kenmore at six-thirty.

All members of the medical profession are cordially invited to attend.

WILLIAM D. MCFEE, M.D., *Secretary.*

THE ARLINGTON DOCTORS' CLUB

The regular meeting of the Arlington Doctors' Club will be held at the Ring Sanatorium on Tuesday, January 14, at 8:30 P.M.

The Belmont Doctors' Club has been invited to attend.

The speaker will be Dr. Conrad Wesselhoeft, Associate Professor of Communicable Diseases, Harvard Medical School, and Medical Director of the Haynes Memorial Hospital.

His subject will be "Problems in Scarlet Fever."

All physicians are invited to attend.

FRANK H. GERRY, *President.*
SIDNEY M. SIMONS, *Secretary.*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital Amphitheatre (Shattuck Street Entrance), Tuesday evening, January 14, at 8:15 P.M.

PROGRAM

Presentation of Cases.

The Physiology of the Elephant. By Dr. Francis G. Benedict.

Medical students and physicians are cordially invited to attend.

MARSHALL N. FULTON, M.D., *Secretary.*

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, JANUARY 13, 1936

Tuesday, January 14—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. Cases from Blood Clinic. Dr. Isadore Olef.

2:30 P.M. Pediatric Ward Visit. Massachusetts Eye and Ear Infirmary.

7:45 P.M. Gardner Auditorium, State House, Boston. Adults in Difficulty. A. Warren Stearns, M.D.

*8:15 P.M. Harvard Medical Society. Peter Bent Brigham Hospital Amphitheatre (Shattuck Street Entrance).

*8:30 P.M. The Arlington Doctors' Club at the Ring Sanatorium.

Wednesday, January 15—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. Modification of History Taking and Physical Examination Methods in Pediatrics. Dr. Francis McDonald.

†12 M. Clinico-Pathological Conference. Children's Hospital.

*8 P.M. New England Physical Therapy Society. Hotel Kenmore, Boston.

Thursday, January 16—

*8:30-9:30 A.M. Clinic, Surgical and Orthopedic Staffs of Children's Hospital, at the Children's Hospital.

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. Social Service Case Presentation. Miss Edith Canterbury.

*2.30 P.M. Medical Clinic at the Peter Bent Brigham Hospital.

Friday, January 17—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. The Diagnosis and Management of Biliary Tract Disease. Frank Lahey, M.D.

12 M. Massachusetts General Hospital, Clinical Meeting of the Staff of the Children's Medical Service. Ether Dome.

Saturday, January 18—

*9-10 A.M. Boston Dispensary, 25 Bennet Street, Boston. Presentation of Ward Cases. Dr. H. C. Gordonier.

*10-12. Staff rounds at the Peter Bent Brigham Hospital.

Sunday, January 19—

4 P.M. Free Public Lecture, Harvard Medical School, Building D, Longwood Avenue. The Prevention of Infectious Diseases. Dr. H. C. Stuart.

*Open to the medical profession.
†Open to Fellows of the Massachusetts Medical Society.

January 9-31—Boston Dispensary Medical Conference Program. See page 87.

January 10—William Harvey Society will meet in the Auditorium of the Beth Israel Hospital, Boston, at 8 P.M.

January 14—Harvard Medical Society. See page 91.

January 14—The Arlington Doctors' Club. See page 91.

January 15—New England Physical Therapy Society. See page 91.

January 16—Medical Clinic at the Peter Bent Brigham Hospital. See page 87.

January 17—A Lecture by Dr. E. V. McCollum (Worcester County Home Economics Association). See page 87.

January 21—South End Medical Club. See page 91.

January 21—Lawrence Cancer Clinic. See page 87.

January 27—Springfield Medical Association.

February 24 to May 16—International Medical Postgraduate Courses in Berlin. See page 1211, issue of December 12, 1935.

March 2-6—The American College of Physicians. See page 91.

June 15-19—The Executive Board of the Catholic Hospital Association will meet at the Fifth Regiment Armory, Baltimore, Md.

September, 1936—First International Conference on Fever Therapy. See page 1325, issue of December 26, 1935.

DISTRICT MEDICAL SOCIETIES

ESSEX SOUTH DISTRICT MEDICAL SOCIETY

February 5—Council Meeting, Boston.

February 12—Wednesday. Addison Gilbert Hospital, Gloucester. Clinic 5 P.M. Dinner 7 P.M. Speaker and subject to be announced later.

March 4—Wednesday. Lynn Hospital. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Timothy Leary. Subject: Arteriosclerosis.

April 1—Wednesday. Essex Sanatorium, Middleton. Clinic 5 P.M. Dinner 7 P.M. Speaker: Dr. Richard H. Overholt of the Lahey Clinic. Subject: Chest Surgery.

May 7—Thursday. Censors' Meeting.

May 13—Wednesday. Annual Meeting. Salem Country Club. Dinner at 7 P.M. Speaker: Dr. Paul White. Subject to be announced later.

R. E. STONE, M.D., Secretary.
88 Lothrop Boulevard, Beverly.

FRANKLIN DISTRICT MEDICAL SOCIETY

Meetings are held on the second Tuesday of January, March and May at the Weldon Hotel, Greenfield, at 11 A.M.

CHARLES MOLINE, M.D., Secretary.
Sunderland.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

Meetings to be held at the Bear Hill Golf Club at 12:15 P.M.

March 11, May 6.

K. L. MACLACHLAN, M.D., Secretary.
1 Bellevue Avenue, Melrose.

NORFOLK DISTRICT MEDICAL SOCIETY

January 28—Hotel Kenmore at 8 P.M. Subject: "Compulsory Sickness Insurance." Speakers to be announced.

February 25—Massachusetts Memorial Hospitals at 8 P.M. Papers by the staff.

March 31—Hotel Kenmore, at 8 P.M. Dr. Benedict F. Boland—"Cauterization of the Cervix Uteri Using Various Electrical Methods." Illustrated with lantern slides.

May—Annual Meeting. (Place, date and subject to be announced.)

The censors meet for the examination of candidates: May 7, 1936; November 5, 1936.

FRANK S. CRUICKSHANK, M.D., Secretary.
1236 Beacon Street, Brookline.

PLYMOUTH DISTRICT MEDICAL SOCIETY

January 16—Goddard Hospital.

March 19—Plymouth County Sanatorium, South Hanson.

April 16—Brockton Hospital.

May 21—Lakeville State Sanatorium.

G. A. MOORE, M.D., Secretary.
167 Newbury Street, Brockton.

SUFFOLK DISTRICT MEDICAL SOCIETY

January 29—Joint Meeting with the Boston Medical Library at 8 Fenway. "Observations Around the World," Dr. Walter B. Cannon.

March 18—Meeting at the Boston Medical Library. "The Laboratory and Clinical Story of Fatigue," Dr. Arlie V. Bock and Dr. David B. Dill. Discussion: Dr. Donald J. MacPherson and Dr. Augustus Thorndike, Jr.

April 29—Annual Meeting at the Boston Medical Library. "The Treatment of Septicaemia," Dr. Champ Lyons. "The Pleurality of Scarlatinal Streptococcus Toxin," Dr. Sanford B. Hooker. Discussion: Dr. Hans Zinsser.

The medical profession is cordially invited to attend all of these meetings.

ROBERT L. DeNORMANDIE, M.D., President,
CHARLES C. LUND, M.D., Secretary,
FRANCIS T. HUNTER, M.D.,
Boston Medical Library.

WORCESTER DISTRICT MEDICAL SOCIETY

February 12—Wednesday evening. Worcester State Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

March 11—Wednesday evening. Memorial Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

April 8—Wednesday evening. Hahnemann Hospital, Worcester, Mass. Dinner and scientific program. Subjects of program to be announced later.

May 13—Wednesday afternoon and evening. Annual Meeting of Society. Time, place and details of program to be announced in an April issue of the Journal.

ERWIN C. MILLER, M.D., Secretary.
27 Elm Street, Worcester.

BOOKS RECEIVED FOR REVIEW

Surgery: Queen of the Arts, and Other Papers and Addresses. William D. Haggard. 389 pp. Philadelphia and London: W. B. Saunders Company. $5.50.

Prescription Writing and Formulary. The Art of Prescribing. Charles Solomon. 351 pp. Philadelphia, London, and Montreal: J. B. Lippincott Company.

An Introduction to Public Health. Harry S. Mustard. 250 pp. New York: The Macmillan Company. $2.50.